the Blumgart-Berlin group would want to claim priority for total thyroidectomy for heart disease, the implication being that many therapeutic measures which at first appear to yield brilliant results are later proved of more doubtful value. We have reluctantly come to the same conclusion. Personal observations since the publication of our first report, an analysis of the recent literature and the results of a questionnaire recently sent to the fifty-five groups and persons who furnished the material for our previous report have caused us materially to alter our previous conclusions as to the value of total thyroidectomy for cardiac disease.

THE RATIONALE OF TOTAL THYROIDECTOMY FOR CARDIAC DISEASE

The association of cardiac disorders with thyrotoxicosis and their disappearance after its proper treatment was the basis of Kocher's [2] suggestion in 1902 that toxic thyroid disease be treated by total thyroidectomy. These observations, however, were made from the viewpoint of thyrotoxicosis. It was not until fairly recent years that the reciprocal relation between thyroid activity and cardiac failure began to be observed. In 1925, Christian [3] stated that "a lowered metabolic activity from thyroid deficiency may be a conservative process, a form of cardiac rest that is advantageous to the heart." Soon afterward, the studies of Blumgart and associates [4] and of Burwell and associates [5] demonstrated that the velocity of the blood flow is proportionate to the metabolic demands of the organism and that these demands, in turn, are greatly influenced by thyroid activity.

In myxedema the velocity of the blood flow and the basal metabolic rate are both low. In hyperthyroidism both are increased. In each of these conditions there is no evidence of cardiac decompensation. In congestive heart failure, on the other hand, there is a discrepancy or

2. Kocher, A.: Ueber Morbus Basedowi, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **9**:1-304, 1902.

3. Christian, H. A.: The Heart and Its Management in Myxedema, Rhode Island M. J. **8**:109-118 (July) 1925.

4. Blumgart, H. L., and Weiss, S.: Studies on the Velocity of Blood Flow: II. The Velocity of Blood Flow in Normal Resting Individuals and a Critique of the Method Used, J. Clin. Investigation **4**:15-31 (April) 1927. Blumgart, H. L.; Riseman, J. E. F.; Davis, D., and Berlin, D. D.: Therapeutic Effect of Total Ablation of the Normal Thyroid on Congestive Heart Failure and Angina Pectoris: III. Early Results in Various Types of Cardiovascular Disease and Coincident Pathologic States Without Clinical or Pathologic Evidence of Thyroid Toxicity, Arch. Int. Med. **52**:165-225 (Aug.) 1933.

5. Burwell, C. S.; Smith, S. C., and Neighbors, DeW.: The Output of the Heart in Thyrotoxicosis, with the Report of a Case of Thyrotoxicosis Combined with Primary Pernicious Anemia, Am. J. M. Sc. **178**:157-168 (Aug.) 1929.

disproportionate relation between the metabolic rate and the velocity of the blood flow, the former being normal and the latter being low. It was on the basis of these facts that Blumgart and associates [4] suggested that, since the failing heart cannot be depended on to increase the rate of blood flow, a rational way to overcome the discrepancy between the metabolic rate and the velocity of the blood flow would be to lower the metabolic rate by removing the thyroid gland in toto. In suggesting the same procedure for angina pectoris these authors postulated that since angina is due to the inadequacy of the coronary blood flow in relation to the demands of the heart muscle, removal of the thyroid gland might be expected to reduce the requirements of the heart muscle to such a degree that the coronary blood flow would be adequate.

The physiologic facts are in accord with the hypotheses of Blumgart and associates, but there are nonetheless certain fallacies in their reasoning. The maintenance of the velocity of blood flow, for instance, represents only one factor in the expenditure of cardiac energy. Other factors which also must be taken into consideration include the cardiac output, the blood pressure level and the heart rate. The blood pressure level and the heart rate after thyroidectomy, both at rest and during exercise, do not show significant differences from the preoperative findings. As to the cardiac output, it is difficult to measure, and the findings are often erroneous, especially in patients with congestive heart failure. According to Levine,[6] instead of being increased (and therefore improved) after the operation, it is actually decreased.

Even if the cardiac output could be shown to be improved by the operation, another significant factor must be considered. It is generally agreed that the secretions of the normal thyroid gland are intimately concerned with muscle tone, irritability and contractility and that lack of thyroid secretion affects adversely the amount of work done by skeletal muscle. This is clearly seen in the asthenia of the myxedematous state. Why, then, should not the deficit induced by total thyroidectomy for cardiac disease have a similarly adverse effect on the heart muscle? If the general metabolism and the metabolism of the heart muscle are depressed proportionately, there seems to be no good reason for assuming that the net result would be an improvement in the state of the circulation.

Levine [6] expressed also the opinion that the alteration of the relation between the basal metabolic rate and the velocity of the blood flow which is effected by total thyroidectomy does not offer an adequate rationale for the performance of the operation for congestive heart failure. His actual words, "*If* [italics ours] the circulation is improved by this procedure, there must be other factors at work," seem to imply that the

6. Levine, S. A.: Clinical Heart Disease, Philadelphia, W. B. Saunders Company, 1936.

operation perhaps does *not* improve the circulation. With this implication and with Levine's further statement that the pathologic physiology of the problem is still unsettled, we are in entire accord. As a matter of fact, we are now of the opinion, as the result of additional observation, that there is no rational basis for assuming that patients with congestive heart failure receive anything but temporary improvement from total thyroidectomy, aside from the improvement inherent in the greatly reduced activity which accompanies the state of myxedema. This temporary improvement is partly psychic and is partly the result of the unusually good preoperative and postoperative care which patients submitted to this operation always receive.

It is true that most patients with congestive heart failure who are submitted to total thyroidectomy have previously failed to respond to medical measures and are likely to have been treated by rest in bed with a minimum of activity for some time before operation. On the other hand, the induction of myxedema by surgical means reduces them to what might be termed subminimal activity, and they benefit accordingly, much as the patient with long-standing cardiac failure may be improved by the administration of a sedative such as morphine. The question then arises whether the degree of improvement to be expected by this mechanism in congestive heart failure compensates for the harmful effects of complete myxedema, which is a rather unhappy state. We no longer believe that it does. We are now of the opinion that total thyroidectomy should not be done on this indication, even in the most carefully selected cases. We have not ourselves employed this operation for congestive heart failure since 1936, and we do not intend thus to employ it in the future.

In a previous communication, one of us (W. K. P.) [7] pointed out that although the theory of Blumgart and associates might possibly explain the results obtained by total thyroidectomy for congestive heart failure, the logic was somewhat strained when applied to angina pectoris. Much more reasonable, in our opinion, is the theory of Levine and associates that the mechanism of relief lies in reflex and humoral alterations, possibly linked with alterations in the adrenal gland.

Angina is a spasmodic disease in which nervous and mental factors play a large part in the production of attacks. It occurs chiefly in persons who have what Houston [8] termed the "spasmogenic aptitude." Coronary disease, although frequently present in association with angina pectoris, is not a major factor in its causation. Coronary disease is frequently

7. Purks, W. K.: Total Thyroidectomy in the Treatment of Congestive Heart Failure and Angina Pectoris, New Orleans M. & S. J. **87**:464-466 (Jan.) 1935.

8. Houston, W. R.: Spasmogenic Aptitude, M. Clin. North America **12**:1285-1302 (March) 1929.

observed in the Chinese and Negro races, in which angina is actually rare. Markedly diseased coronary vessels, which sometimes are completely occluded, are often observed at autopsy in persons who never had angina or even any cardiac pain. In other words, although coronary disease is frequently or even usually found in subjects with angina pectoris, an additional factor of spasm is, in our opinion, necessary to the production of attacks. By the same reasoning, we believe that the relief of angina pectoris frequently obtained by total thyroidectomy can be explained by the complete alteration which the operation produces in the patient's personality and in his reactions to various external and internal stimuli. In short, the person with angina pectoris, as the result of the operation, loses his "spasmogenic aptitude," a concept which agrees in principle with the theory of Levine and associates.

Weinstein and associates [9] attempted to explain the fact that patients with angina pectoris in many instances (40 per cent in their own cases) are relieved from pain immediately after total thyroidectomy, long before any change has taken place in the metabolic rate or the velocity of blood flow. They considered it due to the incidental cutting, in the course of the operation, of sympathetic nerve pathways from the heart which pass through tissues adjacent to the thyroid gland, but in our opinion this theory cannot be accepted without reservations. There is considerable divergence of opinion as to whether these nerves, if they are so located, carry afferent impulses from the heart, and the whole question of the relation of the cervical and upper thoracic sympathetic nerves to anginal pain is open to debate. Satisfactory relief of anginal pain by sympathectomy is accomplished only by widespread surgical intervention, and it is difficult to see why one would "accidentally" accomplish in so large a proportion of patients submitted to total thyroidectomy results which painstaking efforts directed along the same line frequently fail to accomplish.

Our own opinion is that the relief of pain which occurs promptly after total thyroidectomy for angina pectoris can more reasonably be explained on the basis of a psychic factor. In the eyes of the patient the operation carries hope of relief from an otherwise hopeless distressing disease, and he therefore approaches it with great optimism. An additional explanation for at least part of the relief of anginal pain after operation is the period of partial narcosis which precedes and follows the procedure.

All of the factors which might be considered in discussing the rationale of total thyroidectomy for cardiac disease have not, of course,

9. Weinstein, A. A.; Davis, D.; Berlin, D. D., and Blumgart, H. L.: The Mechanism of the Early Relief of Pain in Patients with Angina Pectoris and Congestive Failure After Total Ablation of the Normal Thyroid Gland, Am. J. M. Sc. **187**:753-773 (June) 1934.

been mentioned, but in brief summary it might be said that the mechanism of the relief of congestive heart failure and angina pectoris is based on different factors, aside from the excellent preoperative and postoperative care common to both conditions. In congestive heart failure these factors are: (1) early psychic improvement; (2) reduction of physical activity to a subminimal level by the production of the myxedematous state. In angina pectoris they are: (1) a psychic factor, which accounts for the relief frequently observed soon after operation; (2) an alteration of the patient's personality and a loss of the "spasmogenic aptitude," which account for late improvement.

SELECTION OF CASES

As with all procedures, the selection of cases for total thyroidectomy is of extreme importance. The trial and error method was necessarily applied when the operation was first introduced, and it is now freely admitted by all proponents of the operation that many mistakes were made. There is now rather general agreement that the sole responsibility for the choice of patients suitable for the operation should rest on the cardiologist and that he should be chiefly responsible also for the preoperative and postoperative care. It must also be emphasized, as has previously been pointed out, that when this operation is performed, one disease is substituted for another. If the patient with complete myxedema falls later into the hands of physicians either unable or unwilling to supervise his postoperative care, which in fact covers the remaining years of his life, his last state may indeed be worse than his first.

It is generally agreed that no patient with cardiac disease should be subjected to total thyroidectomy until all possible medical measures have been thoroughly tested and have been proved to be of no value. Before this point can be determined, a long period of preoperative observation and adequate medical care is essential. Only in this way can the correct status of the patient be ascertained, since all chronic maladies are subject to natural variations in intensity.

Finally, there is general agreement that all patients submitted to total thyroidectomy should present at least a fair surgical risk. For this reason it is often necessary to delay operation a considerable time, pending improvement in the patient's general condition.

Although we are now of the opinion that the operation is of little or no value in the treatment of congestive heart failure, the criteria by which cases of this kind are selected should nevertheless be mentioned. Levine [6] summed up the whole matter well when he wrote:

> . . . In those suffering from extremely advanced lesions, if improvement occurs, it may not last long enough to warrant the operation. On the other hand, the

operation does not seem justified if the disease is only slight or moderate or if the disability is not great. There remains a small group of cardiacs, neither too sick nor too well, who may be suitable for the operation.

Clark, Means and Sprague,[10] whose criteria are essentially in accord with those of Blumgart and his group, established certain contraindications for the operation and regard as suitable for it all intractable subjects who do not fit into them. These contraindications include: inadequate previous medical care; *rapid* decline in spite of medical care; continuing severe decompensation in spite of adequate medical treatment (for example, the development of persistent ascites or hydrothorax); valvular lesions accompanied by high venous pressures; low metabolic rates; chronic pulmonary disease of any type; severe nephritis; malignant hypertension; active rheumatic infection. We agree entirely with these contraindications, and we further feel that they restrict almost to the vanishing point the cases of congestive heart failure in which the operation should be performed, even if benefit could reasonably be expected from it.

Most of the contraindications listed for patients with congestive heart failure apply also to patients with angina pectoris, though naturally they are not so likely to occur in patients with angina. The hypothetic subject in whom the best results might be expected from the operation would be a man between 40 and 60 years of age who has had angina for at least nine months, whose attacks are sufficiently frequent to prevent his following a gainful occupation, who has received adequate medical care but whose attacks have not been controlled by this treatment, who does not have a prohibitive amount of organic damage either in the heart or in the vascular system generally and who presents evidence that he is of the type with a high emotional level, as suggested by the term "spasmogenic aptitude." If the patient uses tobacco, he should not be submitted to operation until he has had a trial period without it.

Not many patients, obviously, will meet these criteria. The majority of persons with angina pectoris can be controlled by appropriate medical measures, including due consideration of the emotional factors, while at the other extreme are patients in whom organic damage may be prohibitive. In the selection of cases clinical judgment is probably the best guide, based on: (1) absence of the contraindications listed; (2) only moderately advanced organic cardiac changes; (3) classification in the group of patients with high emotional levels (expressed or latent); (4) attacks of sufficient severity or frequency to cause complete disability.

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10. Clark, R. J.; Means, J. H., and Sprague, H. H.: Total Thyroidectomy for Heart Disease: Experiences with Twenty-One Patients at the Massachusetts General Hospital, New England J. Med. **214**:277-294 (Feb. 13) 1936.

DEATH AND IMMEDIATE COMPLICATIONS

Since total thyroidectomy for cardiac disease is a formidable procedure, it follows that it should be undertaken only by surgeons thoroughly familiar with the anatomy of the region and with a reasonable experience in operations on the thyroid. The technical procedure varies in certain important details from subtotal resection and must be planned deliberately, step by step. The technic has been well described by Berlin, Cutler and others, and the description need not be repeated at this time, but one or two precautions may profitably be mentioned. The incision must be adequate; this means that the prethyroid muscles must invariably be divided. Great care must be exercised to remove every vestige of thyroid tissue, while at the same time carefully protecting the nerves and parathyroid bodies. Our own preference is for local analgesia or nerve block rather than for any form of general anesthesia.

Since the risk of operation for thyrotoxicosis does not exist in total thyroidectomy done on the indication of heart disease, it is the almost universal and a most desirable practice to perform the operation in one stage, even though the patients do not present in any sense ideal surgical risks. The risks inherent in the operation are accounted for in large measure by their poor condition plus the necessity of invading a danger zone ordinarily avoided in the subtotal operation. On the other hand, our own limited experience, as well as the far more extensive experience of others, shows that total thyroidectomy, even when performed on persons with serious and extensive cardiac disease, does not carry a sufficiently great risk, either of death or of complications, to deter one from applying it when it is indicated.

Comparisons with the mortality rate of the subtotal operation naturally suggest themselves. In the removal of the normal thyroid gland there is no risk of the development of a thyroid crisis, which Lahey [11] stated to be responsible for 40 per cent of the 111 deaths in his personal series of 15,300 subtotal operations. There is also little risk of the development of emboli; these were responsible for 10 per cent of the deaths in Lahey's subtotal operations, but they rarely occur after operation on the thyroid except in the presence of auricular fibrillation, which is not usual in angina pectoris and coronary disease. Heart failure is naturally a possibility in patients with congestive failure, but at that, as we pointed out in our first communication on this subject, we are surprised at the relatively low mortality rate associated with total thyroidectomy for congestive heart failure and the extremely low mortality rate for operations for angina pectoris. In our collected series, we found the mortality rates to be 10.48 per cent in 229 operations performed for congestive heart failure and 3.75 per cent in 133 operations performed for angina pectoris.

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11. Lahey, F. H., in discussion on Parsons and Purks.[1]

In the 362 cases which we collected and studied in our previous communication, it was possible to secure exact data concerning complications in 291. The chief risks are naturally injury to the laryngeal nerve or nerves, and/or removal of the parathyroid bodies with consequent tetany. Myxedema, which is an undesirable consequence of subtotal thyroidectomy, is inevitable and desirable following total ablation of the gland.

Twenty-four of the 291 patients in the collected series (8.2 per cent) suffered injury to the recurrent laryngeal nerve. The injury was always unilateral and was usually transient. Scott,[12] in a recent communication concerning total thyroidectomy in 71 cases of diffuse toxic goiter, had 2 such injuries (2.8 per cent); both were unilateral, and both were permanent.

Tetany occurred in 30 cases (10.3 per cent) of our collected series but fortunately was transitory in all but 1 instance, in which it was apparently the cause of death. Scott reported 3 instances of tetany in his 71 cases (4.2 per cent). One instance was mild; 1 required treatment for a year, and 1 terminated fatally. We have had no instance of either tetany or nerve injury in our personal cases of total thyroidectomy.

END RESULTS

There are several reasons for believing that our former conclusions as to the value of total thyroidectomy for cardiac disease were not correct. The first is our personal experience with 4 patients who survived the operation. The 2 patients submitted to the operation for angina pectoris have been followed up since we reported them as doing well in 1937, and they have continued to do well. Neither has been completely rehabilitated, but the results, evaluated conservatively and impartially, may fairly be considered good. The 2 patients with congestive heart failure, however, who also were reported doing well in our first report, have both died, 1 within a year and 1 within three years.

The second reason for our change of opinion is the apparent lack of enthusiasm for the operation at this time on the part of those who formerly recommended and performed it. A review of the literature since 1937 reveals few reported cases. The procedure is evidently being employed in some foreign countries, but the American literature has few articles on the subject, and the initial enthusiasm which colored the early reports is clearly lacking in the papers that are written. Neither Blumgart's nor Levine's group has reported additional cases, and

12. Scott, A. C., Jr.: Total Thyroidectomy for Diffuse (Exophthalmic) Goitre: Preliminary Report of Seventy-One Cases, Tr. Am. A. Study Goiter, 1939, pp. 124-135.

Levine's present skepticism concerning the operation is clear in his recent book on clinical heart disease.[13]

Finally, from a questionnaire recently sent to the fifty-five groups and persons who furnished data for our original collective report, we have received only twenty-five replies, in which only seven reported additional cases. The remaining eighteen replies either express opposition to the procedure or are frankly unenthusiastic about it. For that matter, a similar lack of enthusiasm is apparent in the reports of the seven who have done additional operations. Although it is true that the results of the new cases, when evaluated on the same basis as the cases in the original statistical study, appear to be good, we believe that the failure of cardiologists to recommend and of surgeons to perform additional operations is highly significant.

Our personal experience with the operation since 1937 has been limited to a single patient with angina pectoris, who met the criteria laid down earlier in this paper and in whom the result seems to have been distinctly worth while. We therefore have 3 patients with angina pectoris who survived the operation and in whom the results, observed after sufficiently long periods, have been good.

Good results naturally do not mean that total thyroidectomy is likely to prolong life in patients with angina pectoris. There are no adequate data on which to base such a conclusion. Theoretically, however, it would seem reasonable to expect that life would be prolonged. Any given attack of angina carries a hazard, and the person who suffers two to ten attacks per day is clearly in greater jeopardy than the one who suffers one attack a month or no attacks at all, which is frequently the status of patients who have been submitted to total thyroidectomy. A person with coronary disease, naturally, may suffer coronary occlusion at any time, regardless of whether or not he has anginal seizure.

Since our statistical study in 1937 indicated a considerable probability of relief by total thyroidectomy for both the patient with congestive heart failure and the patient with angina pectoris and since the cases collected in a more recent though less comprehensive questionnaire appear to support the same probability, the question naturally arises as to why we feel that the operation has less merit than the statistical data would

13. Cutler, E. C., and Hoerr, S. O.: Total Thyroidectomy for Heart Disease: A Five-Year Follow-up Study, Ann. Surg. **113**:245-259 (Feb.) 1941. Just after our paper had been completed this excellent article came to our attention. It is based on a careful follow-up study of 57 patients, 16 of whom had survived a five year period of observation. It is of interest that Cutler and Hoerr, on the basis of their extensive experience, concluded that the results of total thyroidectomy for congestive heart failure are disappointing but that the procedure "in a selected group of patients with intractable angina pectoris . . . is a worth while therapeutic measure and is without unwarranted risk."

indicate. We still feel that certain carefully selected patients with angina pectoris might be and actually are benefited by operation, but for several reasons we no longer have the same feeling about the operation for congestive heart failure. The first reason is that if we are to judge by our own experiences, some of the results reported as favorable in our first communication are likely to have proved unfavorable as the period of observation was lengthened. The second reason is, as has already been intimated, that some of the results reported as favorable in our first communication should probably have been discounted because they were obviously colored by the enthusiasm of the men who reported them. The third reason is that if the actual results had been comparable to the statistical evidence of improvement, the literature, instead of a rapidly decreasing number of reported cases, would be likely to show a marked increase, and the persons and groups who supplied the statistical data for our first analysis of the results of total thyroidectomy would show at this time a comparable if not increasing amount of enthusiasm for this mode of treatment.

SUMMARY AND CONCLUSIONS

A statistical analysis of 362 collected cases of total thyroidectomy for cardiac disease, including 5 personal cases, was published in 1937. The mortality rate for the operation performed on the indication of angina pectoris was unexpectedly small, and the results were satisfactory or partially satisfactory in more than 80 per cent of the cases. The mortality rate for the operation performed on the indication of congestive cardiac failure was lower than might have been expected, and the results were satisfactory or partially satisfactory in more than 60 per cent of the cases.

An endeavor to continue the analysis has shown that few cases are being reported in the literature, that cardiologists who formerly recommended the procedure and surgeons who formerly carried it out have apparently lost their enthusiasm for it and that results previously reported as favorable have proved to be less favorable or distinctly unfavorable as time has passed.

Our conclusion at this time, based on a recent analysis of the literature, on a questionnaire sent to the persons and clinics supplying the data for the first report and on personal experience is that total thyroidectomy is of negligible value in the treatment of congestive heart failure, as might be expected in the complete absence of any theory which can reasonably explain why improvement should occur. On the other hand, there is reason to believe that certain carefully selected patients with angina pectoris may be and actually are benefited by the operation, and it should be considered in cases in which medical measures have proved ineffective.

PSEUDOMYXOMA PERITONAEI IN A MAN

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Among the strange pathologic curosities are mucocele of the appendix and its even rarer companion, pseudomyxoma peritonaei. We are convinced from conversations with several surgeons that these conditions are more frequently encountered than recognized. When one considers the high percentage of appendixes in which the lining mucosal cells continue to secrete in the presence of a lumen obliterated at some point, one marvels that this combination of circumstances does not result more often in mucous distention of the organ or, as Féré [1] in 1876 named the condition, mucocele of the appendix.

Rokitansky,[2] in 1842, and Virchow,[3] in 1863, were the first to discover mucocele of the appendix and considered it a colloid degeneration of carcinoma. Werth,[4] in 1884, first recognized and named the condition known as pseudomyxoma peritonaei. Formerly considered to be exclusively of ovarian origin, it was Fraenkel,[5] in 1901, who, observing pseudomyxoma peritonaei in a male patient, realized that it could arise from a mucocele of the appendix. In 43,000 appendectomies at the Mayo Clinic reviewed by Woodruff and McDonald,[6] 146 mucoceles of the appendix were encountered. Castle's [7] figures from 13,158 postmortem examinations place the occurrence at 0.2 per cent of all cases of disease of the appendix.

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1. Féré: Mucocèle de l'appendice ilío-cæcal, Progrès méd. **5**:73, 1876.

2. Rokitansky, C., cited by Weaver.[8]

3. Virchow, R.: Virchows Arch. f. path. Anat. **27**:250, 1863; cited by Weaver.[8]

4. Werth: Klinische und anatomische Untersuchungen zur Lehre von der Bauchgeschwülsten und der Laparotomie, Arch. f. Gynaek. **24**:100, 1884.

5. Fraenkel, E.: Ueber das sogennante Pseudomyxoma peritonei, München. med. Wchnschr. **48**:965, 1901.

6. Woodruff, R., and McDonald, J.: Benign and Malignant Cystic Tumors of the Appendix, Surg., Gynec. & Obst. **70**:750, 1940.

7. Castle, O. L.: Cystic Dilatation of the Vermiform Appendix, Ann. Surg. **61**:582, 1915.

Weaver [8] mentioned 256 reported cases of mucocele of the appendix up to 1937, in 49 of which pseudomyxoma peritonaei resulted. Of these cases, the patients were male in only 14. Since 1937, when Weaver,[8] Morgan [9] and Voigt [10] independently reported cases of pseudomyxoma peritonaei of appendical origin, no cases have been reported in the English literature. We became interested in the subject when we recently encountered a case of mucocele of the appendix with pseudomyxoma peritonaei in a male patient. In this case, the clinical diagnosis, the pathologic picture and the surgical procedure were carefully considered. We believe that this is the fifteenth case of its kind ever published.

CAUSATION

Although the causation of mucocele of the appendix and pseudomyxoma peritonaei is still largely a matter of conjecture, most authors are agreed on several feasible theories. Between the age groups of 25 to 60, when the appendix is involuting, or at any time following healing from recurrent exacerbations of acute appendicitis, the lumen, usually at the proximal end, may become obliterated. Continued secretion of mucus results in distention of either a part or the whole of the appendix. Most authors have expressed the opinion that the mucosa must be sterile in order to form a mucocele. Lifvendahl and Ries,[11] however, suggested that residual low grade inflammation may stimulate the mucous glands to secrete. Grodinsky and Rubnitz [12] concurred with this idea from their experimental work with rabbits in which they produced mucoceles in appendixes which were flushed clean but not sterile before ligation.

Because of increased intraluminal pressure, the mucosa may herniate through the weakened muscle wall as diverticula, which may eventually rupture. When the exudate is deposited in the peritoneal cavity, loose lining cells of the appendix are thrown out; the materials disseminate more or less widely, depending on their volume and the reaction of the peritoneum. Having discharged its content, the appendix may then collapse and the perforation heal. This sequence of events may recur repeatedly over a period of years. Our experience adds nothing to what is recorded in the literature to enlighten the mystery of a time interval relation between the formation of a mucocele of the appendix and the

8. Weaver, C. H.: Mucocele of the Appendix with Pseudomucinous Degeneration, Am. J. Surg. **36**:523, 1937.

9. Morgan, J. O.: Mucocele of the Appendix, J. M. A. Alabama **7**:14, 1937.

10. Voigt, W. W.: Pseudomyxoma Peritonei and Its Ultimate Development, Illinois M. J. **71**:172, 1937.

11. Lifvendahl, R. A., and Ries, E.: Open Communication Between Mucocele and Cecum, Am. J. Surg. **17**:270, 1932.

12. Grodinsky, M., and Rubnitz, A. S.: Mucocele of the Appendix and Pseudomyxoma Peritonei, Surg., Gynec. & Obst. **73**:345, 1941.

appearance of a recognizable pseudomyxoma peritonaei. Perhaps much depends on the ability of the implanted cells to secrete.

Being a foreign body, the thick mucoid material from the appendix sets up chronic serositis when it comes in contact with the peritoneum. As the mucus forms in excess of absorption, fibrin from the serum secreted by the serosa surrounds droplets of the material and divides them into individual ball-like units admixed with columnar epithelial cells. Grodinsky and Rubnitz [12] showed that a ground filtrate of pseudomyxoma peritonaei from 1 rabbit injected into the peritoneal cavity of other rabbits was incapable of forming pseudomyxoma peritonaei. The reverse was true when the mucoid exudate containing intact epithelial cells was implanted. On the other hand, as far back as 1910, Trotter [12a] suggested that the mucoid exudate from the appendix stimulated a metaplasia of the endothelial cells of the peritoneum into a tall columnar form with the ability to secrete. Although this theory is not popular, it is unlikely that it can be disproved on scientific grounds with regard to the human being. The possibility that the implants are the result of a combination of these factors, in at least a few cases, must be considered.

PATHOLOGIC APPEARANCE

The gross pathologic appearance of pseudomyxoma peritonaei may be readily recognized, although the extent of peritoneal involvement and the degree of distortion of the appendix vary considerably in the cases reviewed. It is rare for a case in which the condition is minimal or in an early stage to be described, since only when the condition is well advanced does it cause symptoms. The mucocele may vary from 3 cm. in length to the size of a football. Regardless of the size of the mucocele of the appendix, its rupture is necessary to form pseudomyxoma peritonaei. This is emphasized by the fact that some of the largest mucoceles have been unassociated with pseudomyxoma peritonaei. A feature often encountered by surgeons is the occurrence of one or more completely walled-off, mucoid-filled cysts varying greatly in size. These cysts may be close to the appendix or some distance from it. Attempted removal of them has not infrequently resulted in rupture of a thin-walled portion. Morgan [9] reported a case of an inoperable single cyst filling the entire abdomen, from which a total of 21 liters was removed. Later, it was demonstrated that this cyst was separate from the appendix. In our case, no cysts other than the mucocele existed, although advanced pseudomyxoma peritonaei was evident.

The wall of the appendix undergoes some fibrous thickening as if in response to chronic inflammation. Classically, the lumen at the proximal

12a. Trotter, W.: Peritoneal Pseudo-Myxoma Originating from the Vermiform Appendix, Brit. M. J. **1**:687, 1910.

end is closed. Dodge,[13] however, mentioned 5 cases in which the lumen was patent. It is conceivable that in these cases the pressure of the accumulated mucus could have forced itself through a preexisting channel into the cecum. This seems likely, for in none of Dodge's cases did a mucocele rupture into the peritoneum to form pseudomyxoma peritonaei.

Histologic sections of mucocele of the appendix show pictures which vary from areas of normal mucosa to a thickened fibromuscular wall lined by hyperplastic and hypertrophied cylindric epithelial cells, some of which may be actively secreting. If the appendix is greatly distended, many areas may be devoid of mucosa from pressure atrophy. Some round cell infiltration is often present.

Grossly, the tenacious matter of pseudomyxoma peritonaei is found free and implanted on the peritoneal surfaces. In most cases the exudate is confined to a small area of the right lower quadrant of the abdomen. In a few of the reported cases, the process was more widely disseminated, involving, as it did in our case, the viscera of all quadrants of the abdomen, the mesentery of the bowel and the peritoneum. Regardless of the extent of the lesion, the exudate (fig. 1) grossly consists of golden yellow gelatinous mucoid material, referred to commonly as "frog spawn" or "fish eggs," admixed with a cloudy serous fluid.

Typically, in sections of the frog spawn exudate (fig. 2), one sees fibrin and abundant eosin-staining mucinous material through which are occasionally scattered long chains of tall columnar epithelial cells tending to form large cysts.

Pseudomyxoma peritonaei has not been well discussed from the histologic point of view, and in many cases, pseudomyxoma peritonaei originating from mucocele of the appendix has been considered to be malignant on clinical grounds, but there has been no histologic description of the implants in these cases. Having excellent operative and postmortem specimens, we have endeavored to determine: (1) the similarity, if any, to pseudomyxoma peritonaei derived from cystadenoma of the ovary; (2) whether the process was of neoplastic or inflammatory nature, and (3) what, if any, contributions it makes to the patient's death. In our case, evidence was presented of suggestive malignant degeneration occurring in pseudomyxoma peritonaei along with benign mucocele of the appendix.

Not enough investigative work has been done to compare properly the features of pseudomyxoma peritonaei of ovarian origin with those of the process of appendical origin. In the most recent work by von Nánay[14] in a German paper, mucocele is considered the source

13. Dodge, G. E.: Cystic Dilatation of the Appendix, Ann. Surg. **63**:334, 1916.

14. von Nánay: Die Rolle der Wurmfortsatzzysten in der Entstehung der Pseudomyxoma Peritonei, Beitr. z. klin. Chir. **171**:74, 1940.

of pseudomyxoma peritonaei, and tumors of the ovary are mentioned only in passing as the cause usually attributed. Pseudomyxoma peritonaei is usually of ovarian origin, but some authorities[15] have expressed the opinion that in many cases a mucocele of the appendix may have been overlooked. Voigt[10] recalled that in cases of pseudomyxoma peritonaei, mucocele of the appendix and cystadenoma of the ovary often occur simultaneously. Reinike[15a] observed that in female patients with pseudomyxoma peritonaei, if both the appendix and the ovarian tumor were not removed, recurrences of pseudomyxoma peritonaei were more rapid. Based on work by Masson and Hamrick[16] on ovarian pseudomyxoma peritonaei and on opinions by several other authors concerning the appendical origin of the condition, the following comparison is offered:

Pseudomyxoma Peritonaei Originating in Mucocele of the Appendix	Pseudomyxoma Peritonaei Originating in Ovarian Cystadenoma
Origin: Mechanical obstruction of the lumen and rupture of a mucocele	Neoplasm: rupture of the cyst
Clinical course: More benign	More malignant
Prognosis: Better	Worse
Histologic nature of implants: Malignant in 38 per cent; not so cellular; chains of single cells	Malignant in 43 per cent; more cellular; alveolar and papillomatous tendencies present in many
Gross characteristics: Single mucocele	Bilateral ovarian tumors in 50 per cent; bilateral involvement in 73 per cent of the cases in which the process was malignant
Reaction of exudate: Acid	Alkaline

A reasonable search of the literature has not revealed to us whether pseudomyxoma peritonaei can occur in the absence of a ruptured ovarian cystadenoma. It seems that this might be possible, especially in cases of ovarian cystadenocarcinoma, in which cells penetrating as far as the serosa of the cyst could undergo cell division and secretion with the formation of pseudomyxoma peritonaei. Ewing[17] pointed out that ovarian cystadenocarcinoma spreads mainly by peritoneal implants but that it may extend to lymph nodes, such as the retroperitoneal and the inguinal, and, rarely, to distant organs. Lymphatic invasion does not occur with pseudomyxoma peritonaei from mucocele of the appendix.

15. (*a*) Reinike, W.: Problem of Pseudomyxoma of the Peritoneum, Ginek. **8**:347, 1937. (*b*) Morgan.[9] (*c*) Voigt.[10]

16. Masson, J. C., and Hamrick, R. O.: Pseudomyxoma Peritonei of Ovarian Origin: Analysis of Thirty Cases, S. Clin. North America **10**:61, 1930.

17. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940.

When ovarian tumors produce pseudomyxoma peritonaei, the degree of malignancy varies considerably. Histologically, the implants from ovarian cystadenoma are generally more malignant than are those from mucocele of the appendix. Novak [18] pointed out that even in cases of frankly benign ovarian papillary serous cystadenoma, there can be no certainty as to a benign clinical course.

In none of the articles on pseudomyxoma peritonaei with which we are familiar is colloid carcinoma of the gastrointestinal tract mentioned in the differential diagnosis. Because of the gross appearance of pseudomyxoma peritonaei and its colloid nature, we feel that this condition must have entered the minds of many who encountered it as it did ours. We have been unable to find a single instance of pseudomyxoma peritonaei which has had its origin in colloid carcinoma of the gastrointestinal tract. Little has been written concerning the metastatic peritoneal implants of colloid carcinoma. Two cases reported in the *New England Journal of Medicine* [19] and a section in MacCallum's textbook [20] reveal certain characteristics which distinguish colloid carcinoma from pseudomyxoma peritonaei, namely: (1) definite clinical evidence of a primary lesion in the intestinal tract; (2) metastatic implants less colloid than the primary lesion; (3) absence of any large quantity of freely floating frog spawn exudate; (4) grossly, more invasion and the presence of visceral metastasis; (5) histologic evidence of malignancy.

CLINICAL PICTURE

There is no characteristic clinical syndrome associated with mucocele of the appendix, and indeed the condition is rarely diagnosed preoperatively. Among all the cases reviewed by Dodge [13] and Morgan [9] there was only 1 case of mucocele of the appendix correctly diagnosed preoperatively or before autopsy. Since then, Ruddock [21] has listed mucocele of the appendix as a preoperative diagnosis made by peritoneoscopy. We believe ours to be the third correct preoperative diagnosis, and it, too, was made by peritoneoscopy. In this case, the instrument corrected a previous clinical impression of metastasis of carcinoma of the bowel and led to an elective appendectomy.

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18. Novak, E.: Gynecological and Obstetrical Pathology, Philadelphia, W. B. Saunders Company, 1940.

19. Colloid Carcinoma of Stomach (Primary) with Hepatic and Peritoneal Metastases, Cabot Case 23321, New England J. Med. **217**:270, 1937. Colloid Carcinoma of Stomach with Metastases to Mesenteric and Cervical Lymph Nodes and Bone Marrow, Cabot Case 24411, ibid. **219**:577, 1938.

20. MacCallum, W. G.: Textbook of Pathology, ed. 7, Philadelphia, W. B. Saunders Company, 1940.

21. Ruddock, J. C., in Davis, C. H.: Gynecology and Obstetrics, Hagerstown, Md., W. F. Prior Company, Inc., 1935, vol. 3, chap. 16, p. 3.

Of the cases of mucocele of the appendix in which operation was done, in about half there was a history of pain, discomfort or other vague symptoms referable to the right lower quadrant of the abdomen. In the other half, no symptoms were present. Attacks years previously of acute appendicitis for which no operation was performed characterize the history in many cases. In those resulting in pseudomyxoma peritonaei, painless abdominal swelling, varying in duration from six weeks to three years, loss of weight, exhaustion and anorexia make up the usual picture, although abdominal swelling is the only constant finding. Even this is absent except in cases in which the condition is advanced. Signs of gradual intestinal obstruction frequently occur as a terminal event in cases in which the condition is advanced. Mayo [22] suggested that mucocele of the appendix should be considered whenever there is distress and a palpable mass in the right lower quadrant of the abdomen, especially in a male patient. Mucocele of the appendix has been observed in subjects from 4 to 72 years of age, the average age being 41 years. It is strange that although mucocele of the appendix is more frequent in male patients, it produces pseudomyxoma peritonaei four times as often in females.

PROGNOSIS

The prognosis of uncomplicated mucocele of the appendix is good. From the Mayo Clinic, the younger Charles Mayo [22] reported 70 cases in which simple appendectomy was done for mucocele of the appendix without an operative death. Complete spontaneous regressions of pseudomyxoma peritonaei after appendectomy have been reported. Clinically, most cases are fatal in two to three years after appendectomy in spite of the comfort afforded by courses of postoperative irradiation.

The complications from simple mucocele of the appendix suggested by Jones and Carmody [23] are: (1) intussusception; (2) invagination; (3) volvulus; (4) intestinal obstruction; (5) occurrence in a hernial sac; (6) gangrene; (7) rupture of vessels. Carcinoma and pseudomyxoma peritonaei obviously should be added to this group. Jefferies [24] stated that of all the cases of pseudomyxoma peritonaei fully reported to 1932, in about 62 per cent the process was benign and in 38 per cent, it was malignant. Woodruff and McDonald [6] expressed the belief that pseudomyxoma peritonaei of appendical origin is derived from low grade cystadenocarcinoma of the mucocele and not from benign mucocele. In

22. Mayo, C.: Mucocele of Appendix with Case Report, Minnesota Med. **15**: 254, 1932.

23. Jones, T., and Carmody, M.: Mucocele of Appendix, Am. J. Surg. **31**: 511, 1936.

24. Jefferies, J.: Pseudomyxoma Peritonei, Ann. Surg. **96**:215, 1932.

10 cases included in their review of 146 cases, the mucocele of the appendix was of a low grade of malignancy, and none of the total group produced pseudomyxoma peritonaei. That a mucocele is necessarily malignant seems unlikely in view of the experimental work by Grodinsky and Rubnitz, who produced benign mucocele of the appendix and pseudomyxoma peritonaei in rabbits. The findings in our case substantiate those of others [25] in that no malignancy was observed in the sections made from the mucocele of the appendix in a case in which widespread pseudomyxoma peritonaei was present.

From a histologic standpoint, in most cases pseudomyxoma peritonaei of appendical origin is benign in that actual carcinomatous cellular characteristics have not been reported. However, it should be emphasized that the complications leading to death occur regardless of cellular detail, inasmuch as they are of a mechanical, rather than an invasive, nature. From the clinical and the autopsy study in our case, we are able to suggest several complications of pseudomyxoma peritonaei, any one or a combination of several of which may cause the patient's death: (1) inability of the peritoneum to withstand the slightest infection (this has already been emphasized by Voigt [10]); (2) gangrene of the appendical stump with perforation after appendectomy; (3) intestinal obstruction from incarceration due to compression of the peritoneal exudate around the curling loops of the small bowel; (4) gradual small bowel infarction from impaired portal venous return caused by compression of the exudate on the mesenteric veins; (5) malignant degeneration.

REPORT OF A CASE

A 62 year old white man was admitted to the hospital on Feb. 22, 1941, with a history of five weeks' duration of moderately severe burning pain in the upper part of the abdomen radiating to the left flank, accompanied by progressive abdominal enlargement, constipation and moderate anorexia. He had lost 20 pounds (9.1 Kg.) since the summer of 1940. The past medical history was negative.

Physical examination revealed a fairly well developed but undernourished man with signs of pulmonary emphysema, bilateral elevation of the diaphragm and marked abdominal ascites. Rectal examination revealed a normal prostate. About 4 cm. within the rectum, the examining finger made contact with a uniformly smooth constriction of the lumen which did not have the irregularity and the resistance of carcinoma. A sigmoidoscope could not be passed beyond the first turn of the rectum owing to the resistant constriction. The mucosa appeared normal. No intrinsic lesion was seen.

By roentgen examination, no organic lesion in the colon was demonstrated. It was noted that the junction of the sigmoid and the descending colon did not have a large caliber and was not freely movable. The examination was not satisfactory owing to ascites.

25. Weaver.[8] Voigt.[10]

Laboratory examinations were made with the following results: The urine was normal. The hemoglobin content of the blood was 74 per cent. The red blood cell count was 3,880,000. The white blood cell count was 9,200, with 72 per cent polymorphonuclear leukocytes, 19 per cent lymphocytes, 4 per cent monocytes, 3 per cent eosinophils, 2 per cent basophils and 59 filamented forms and 13 non-filamented forms. The Wassermann and Kahn tests were negative.

As had been the experience of others, there was no clue in this case to aid in making a correct diagnosis. Because lesions of the rectum are rarely demonstrated by roentgen examination and because of the atypical rectal and proctoscopic findings, a tentative diagnosis of carcinoma of the rectum with generalized carcinomatosis was made. With the idea of relieving distention by paracentesis and confirming the diagnosis, the patient was referred to one of us for peritoneoscopy on March 4.

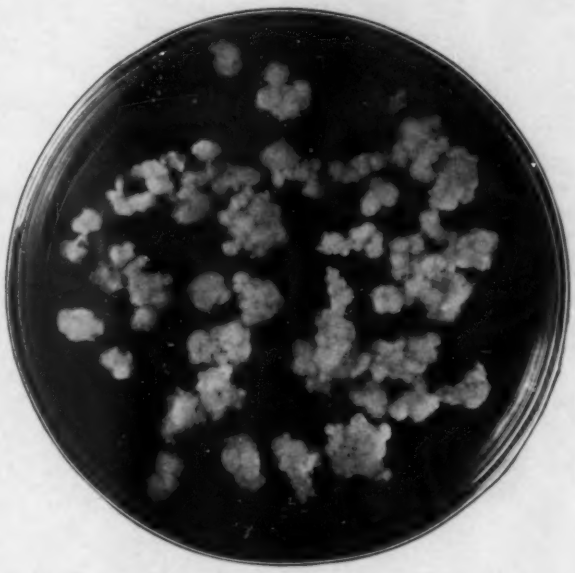

Fig. 1.—Photograph of a culture of pseudomyxoma peritonaei in a Petri dish showing clusters of sharply circumscribed gelatinous material resembling fish eggs. Seven liters of this material was withdrawn through the peritoneoscope sheath.

Peritoneoscopy.—Thick gelatinous blood-tinged fluid (7,000 cc.) admixed with frog spawn-like material was withdrawn through the sheath (fig. 1). The exudate was too thick to have been removed through a tube less than 12 mm. in diameter. Inspection with the peritoneoscope was most satisfactory and revealed multitudinous masses of honey-colored translucent gelatinous material adherent to the parietal peritoneum over the stomach and the omentum. There were a few nodules on the liver, but the remainder of this organ appeared normal. The lesions did not appear firmly attached and implanted as in carcinoma. They gave the impression that a stroke of the finger would easily brush them away. Inspection of the lower quadrants of the abdomen revealed myxomatous implants in every quarter, and with the patient in the Trendelenburg position, there appeared to be a large mass

of the material between the bladder and the rectum. A diagnosis of pseudomyxoma peritonaei was made with the inference that mucocele of the appendix was the most likely source.

Histologic Examination.—The exudate (fig. 2) consisted of pinkish mucinous material admixed with fibrin through which were scattered long chains of well differentiated tall columnar epithelial cells tending to form large cysts or acini.

Fig. 2.—Photomicrograph of peritoneal exudate of pseudomyxoma peritonaei. Note the chain of well differentiated cylindric cells admixed with fibrin and mucinous exudate. A few mononuclear cells and fibroblasts are present. (Hematoxylin-eosin stain; × 450.)

Leukocytes and red blood cells were irregularly scattered. The material gave the chemical reactions for pseudomucin.

For the next twenty-seven days, the patient felt much better, the fluid did not reaccumulate, and he went about his daily work at home free from pain.

Operation.—On March 31, appendectomy was performed with the patient under spinal anesthesia. Through a right paramedian hypogastric incision the peritoneal cavity was entered, and a condition of pseudomyxoma peritonaei was encountered similar to that observed by peritoneoscopy. A large amount of myxomatous material was manually delivered, and extensive infiltration of the omentum was particularly noted. An attempt was made to isolate the appendix, and in the exploration a cystic mass was felt in the pelvis just beyond the pelvic brim on the right side. During delivery, the mass ruptured through a thin-walled portion, evacuating 65 Gm. of clear thick mucinous material. The mass was dissected farther up and was found to be continuous with, or to actually be, the appendix, having its origin at the ileocecal junction. The appendix was removed, and the stump was doubly

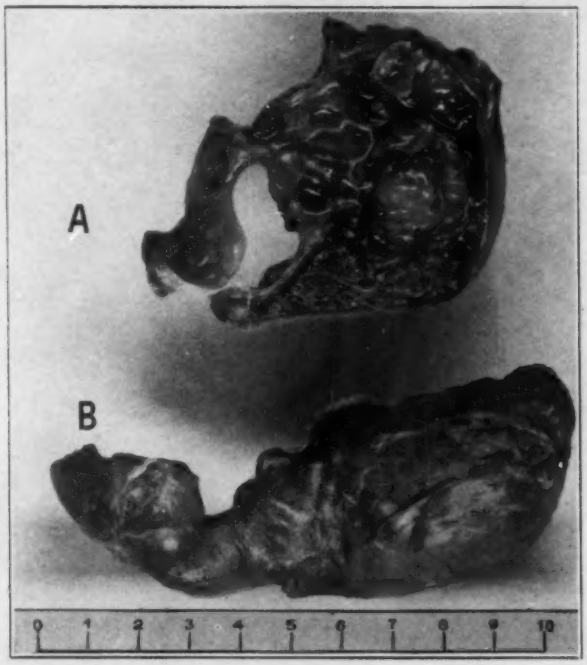

Fig. 3.—*A*, photograph of a portion of the spleen showing thickened capsule and pulp invaded by thick-walled multiloculated cysts filled with golden yellow gelatinous material. *B*, photograph of a mucocele of the appendix (less than actual size owing to mounting). To the left is the thick-walled proximal end with the obliterated lumen; to the right is the thin-walled distended portion which contained 65 Gm. of thick gelatinous mucoid material. (Ruler shows centimeters.)

ligated with no. 1 chromic catgut without being buried. The wound was closed in layers without drainage.

Pathologic Report.—The specimen (fig. 3) consisted of a membraneous sac, 10 cm. long, 4.5 cm. in diameter at the distal end and 2.5 cm. at the proximal end and weighing 33 Gm. The serosa was pinkish and smooth except where adhesions had been torn away or where implants of yellowish mucoid material were attached. The wall of the distal end, which had ruptured, was paper thin. The inside of the sac was smooth except for some trabeculation. The proximal end

was solid, devoid of a lumen and composed of compressed colloid-like islands. It contained the material already described as rupturing during operation. In addition, a biopsy of omentum containing gelatinous colloid material was made.

Microscopic Examination.—Sections of the appendix (fig. 4) cut just distal to the obliterated proximal end revealed recognizable muscularis, but without the crypts of Lieberkühn or the solitary lymphoid follicles. The thickened wall consisted of muscle and well organized hyalinized fibrous tissue. Lining part of the

Fig. 4.—Photomicrograph of a section from the wall of a mucocele of the appendix showing the secreting epithelial cells, the absence of submucosa and the fibrous muscularis. Some of the pseudomyxoma peritonaei is on the outside of the wall (right). Most sections of the appendix did not reveal any mucosa. (Hematoxylin-eosin stain; × 120.)

lumen was a single layer of well differentiated epithelial cells varying in form from low cuboid to tall columnar. The tall columnar cells could be clearly seen to be secreting. The contents were composed of a bluish pink–staining homogeneous mucoid-like material. Except for a few isolated columnar cells, the lining of the rest of the appendix was devoid of mucosa.

The sections used in biopsy of the omentum were similar to the peritoneal exudate removed three weeks previously, except that, in addition, a few goblet cells were present, and there was evidence of secretion. The cells were well differentiated, and there was no appearance of malignancy. Surrounding these cells were broad bands of collagenous and fibrous connective tissue. Some mononuclear cell infiltration and fibrosis confirmed the chronic serositis exerted by the exudate.

Postoperative Course.—For three days after operation, the patient's course was uneventful. After this, signs of gradually progressive chronic intestinal obstruction

Fig. 5.—Photograph showing: in the lower half, the omentum, which weighed 1,300 Gm.; in the upper half, a loop of large bowel turned in the midportion to display smooth mucosa and myxomatous involvement of the serosa; in the upper left, a mucocele of the appendix. (Ruler shows inches.)

without pain developed. The temperature oscillated between 98 and 101.5 F. The patient died twelve days after operation.

Autopsy.—Discussion of the autopsy is limited to the abdomen because the remaining parts were noncontributory to the case or the cause of death.

The abdomen was tense, distended and flat to percussion. On entrance into the peritoneal cavity, a strange pathologic curiosity was encountered. The cavity contained 2,000 cc. sanguineous fluid in which floated flecks of pseudomyxomatous material. The entire peritoneum and the large apron of omentum (fig. 5) obscuring

the viscera were covered by a dense mass of closely knit myxomatous nodules varying in size from 2 mm. to cystic areas 2 cm. in diameter, which contained thick gelatinous clear yellowish material. The omentum weighed 1,300 Gm. and measured 35 by 15 by 4 cm. It was boardlike in consistency and adherent to the underlying viscera.

With the omentum freed, the large and the small bowel were seen to be covered with this same myxomatous process as well as a whitish foul-smelling fibrinopurulent exudate; obviously, generalized acute suppurative peritonitis was present. Handling the viscera resulted in the expulsion of flatus through the peritoneal fluid of the lower right quadrant of the abdomen. The widespread heavy myxomatous exudate so securely encased the viscera that removal of the intestinal tract was extremely difficult owing to the confusion of anatomic landmarks. Segments of the small intestine were kinked by the plastic exudate. It is difficult to understand how bowel contents traversed these loops, yet the small intestinal contents were fluid throughout. The mesentery of the small intestine and the sigmoid was greatly thickened by a coating of the peritoneal exudate. The tone of the small and the large bowel was poor; the color, dark. The cecum was particularly soft, thin walled and dark. A perforation was present at the site of the appendical stump, thus accounting for the flatus and generalized peritonitis. No suture material was seen, and there was no gross gangrene or necrosis about the perforation. The mucosa of the entire gastrointestinal tract was essentially normal (fig. 5), aside from the suggestive degeneration and darkening continuous with this appearance on the serosa of the small intestine. At no point had the myxomatous implants invaded the mucosa.

The liver and the gallbladder were normal aside from the frog spawn implants limited to their external surface. The spleen (fig. 3) weighed 200 Gm. Interposed between the diaphragm and the spleen, connecting the two, were multiloculated thick fibrous-walled cysts filled with yellowish gelatinous material. The splenic capsule was thickened, and the mushy pulp had been invaded in numerous areas by gelatinous material similar in all respects to the abdominal exudate.

The adrenals, the kidneys, the bladder and the pancreas were essentially normal.

Microscopic Examination.—Sections of the stomach and the small bowel revealed noninvasive myxomatous implants and purulent peritonitis confined entirely to the serosa. The large intestine (fig. 6), being more inadequately protected by the omentum, revealed even greater acute peritonitis. The chronicity of pseudomyxoma peritonaei was typified in sections of the large bowel. Here, confined to the serosa, were dense fibrous strands and myxomatous material well supplied by small blood vessels. The clusters of acini were actively secreting. Some neoplastic tendency was present in a few sections of the large intestine (fig. 7). This was characterized by large acini formed of tall deep eosin-staining actively secreting cells with large pale nuclei. Such hyperplasia of cells occurred that solid clusters were formed, and in some areas nothing but nuclei and pale vacuoles were present. Atypical mitosis was observed, as was also invasion beyond a basement membrane. The size and the activity of these cells seemed out of proportion to their theoretic appendical origin.

Spleen.—The walls of the multiloculated cysts were similar to the thickened hyaline splenic capsule. Lining both were single and multiple layers of pleomorphic epithelial cells which did not invade the hyaline wall. In one area (fig. 8), the mucoid exudate could be seen to break through the capsule and into the splenic pulp at two points. This was the only place in all the histologic sections in which an organ had been invaded beyond its surface.

Fig. 6.—Photomicrograph of a section from pseudomyxoma peritonaei covering the serosa of the large bowel; at the top, acute peritonitis is imposed. (Hematoxylin-eosin stain; × 450.)

Fig. 7.—Photomicrograph of a section from pseudomyxoma peritonaei on the exterior of the large intestine showing anaplastic tendency of cells and vacuolation. (Hematoxylin-eosin stain; × 450.)

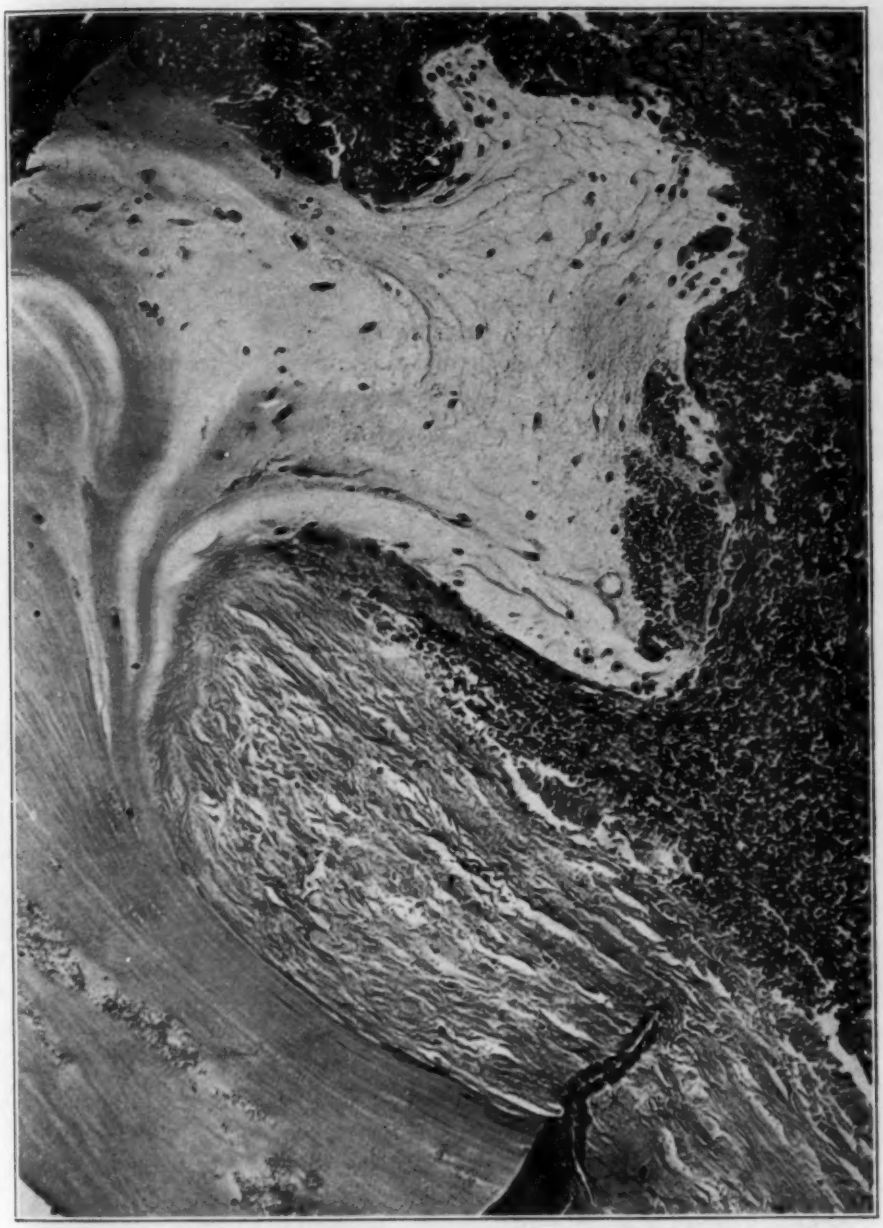

Fig. 8.—Photomicrograph of a section of the spleen showing mucoid exudate penetrating the capsule and extending into the pulp. (Hematoxylin-eosin stain; × 450.)

COMMENT

We cannot be certain that this cell anaplasia indicated a definitely histologically malignant process and will grant that pathologists might well differ in their impressions. That cells from a benign appendical mucosa can be implanted on the peritoneum, grow, secrete and produce cells is evident. That they can become malignant, even though their appendical source remains benign, has been less well understood and offers material for hypotheses.

Any evidence of malignant degeneration is largely one of academic interest in this case. The actual cause of death was a series of related events, namely, perforation of the appendical stump, peritonitis and ileus. It is amazing that this patient could have survived so long with such extensive peritoneal growth, and it is conceivable that he otherwise would have succumbed to compression of the bowel or the mesenteric vessels by the myxomatous material.

TREATMENT

Whether mucocele of the appendix progresses to pseudomyxoma peritonaei or not, the treatment for both conditions is appendectomy. Most operators manually extract as much of the myxomatous material as possible while operating in the peritoneum so that cachexia will not result from too much protein absorption. Closing the abdomen without drainage is advised to reduce the chance of contamination of a peritoneum already reduced in resistance.

Spontaneous rupture of the appendical stump which occurred in our case may serve as a warning to others. During the formation of a mucocele, the tension put on, and the stretching required of, the appendical wall from intraluminal distention may result in a portion of the cecum being drawn toward the appendix in conelike fashion to serve as its proximal attachment. If one then performs an appendectomy in the usual manner, a portion of the cecum is actually cut and ligated. Then after appendectomy, the evaginated cecum tends to assume its previous state, and the tension put on the ligating sutures jeopardizes the integrity of the operative closure. This is undoubtedly what occurred in our case, since no gangrene or necrosis of the stump was found.

Mulsow [26] reported a case in which gangrene of the cecum and the proximal part of the appendix had occurred from invagination of the mucocele into the cecum. These experiences along with the poor tone and color of the bowel noted in our case warn that trouble may be expected in the region of the cecum. With this in mind, Jones and Carmody [23] designed a special operation for mucocele of the appendix.

26. Mulsow, F. W.: Mucocele of the Appendix with Diverticulum and Invagination into the Cecum, Tr. Chicago Path. Soc. **13**:434, 1931.

It consists in removing the lower dependent portion of the cecum, including the appendix, between Payr clamps in such a way that the normal opening of the ileum into the cecum is maintained. Then a Parker-Kerr basting stitch is used to close the opening in the cecum. The reader is referred to the splendid diagrams in the paper of Jones and Carmody.

Finally, roentgen irradiation in cases of pseudomyxoma peritonaei following appendectomy is almost universally advocated. Weaver [8] recommended starting radiation therapy thirty days after operation. His dosage was a series of fourteen treatments totaling 1,386 r over the abdomen and 1,192 over the pelvis divided among twenty-five days.

SUMMARY

The fifteenth case to be recorded of pseudomyxoma peritonaei from mucocele of the appendix occurring in a man is reported.

Although ovarian cystadenoma is the common source of pseudomyxoma peritonaei, mucocele of the appendix should not be overlooked.

Pathologically, the neoplastic tendencies, the mortal potentialities and a comparison of the appendical and ovarian origins of pseudomyxoma peritonaei are discussed.

There are no reliable diagnostic clinical features of either mucocele of the appendix or pseudomyxoma peritonaei. Peritoneoscopy was an aid to diagnosis in this case.

The prognosis of simple mucocele of the appendix with appendectomy is good. Cecectomy, to include the dependent part of the cecum and the appendical attachment, is a rational procedure.

Appendectomy and postoperative irradiation should be done in cases of pseudomyxoma peritonaei. The prognosis, however, is grave. The complications and the cause of death in cases of pseudomyxoma peritonaei are of mechanical origin and are not dependent on the presence of malignant cell characteristics.

Drs. W. P. Belk and E. T. Crossan gave valuable suggestions in the preparation of this paper.

ABSORPTION OF SURGICAL GUT (CATGUT)

III. DURATION IN THE TISSUES AFTER LOSS OF TENSILE STRENGTH

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In previous communications, the decline and the duration of the tensile strength of surgical gut (catgut) in the tissues [1] and in acid-pepsin solution [2] were reported. An important aspect of absorption of surgical gut is the length of time required for complete absorption after the loss of useful holding power in the tissues. Bates [3] made observations on the absorption of the plain and the chromic catgut of various sizes of one manufacturer. Bower, Burns and Mengle [4] carried out studies on the absorption of two different sizes of catgut of another manufacturer. These experimental studies were made over relatively short periods and were not necessarily designed to follow the ultimate fate of the catgut.

It has been observed clinically at secondary operations through healed incisions that chromic catgut of some varieties may sometimes be readily identified months after it was originally placed in the wound. Also, it has been a clinical observation that chromic catgut of some types may lead to a draining sinus in the operative wound which does not heal over completely until a bulky knot of catgut is extruded or removed

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From the Department of Surgery, the University of Chicago School of Medicine.

This work was aided in part by a grant from the Council on Pharmacy and Chemistry of the American Medical Association.

1. Jenkins, H. P., and Hrdina, L. S.: Absorption of Surgical Gut (Catgut): I. The Decline in Tensile Strength in the Tissues, Arch. Surg. **44**:881 (May) 1942.

2. Jenkins, H. P., and Hrdina, L. S.: Absorption of Surgical Gut (Catgut): II. Pepsin Digestion Tests for Evaluation of Duration of Tensile Strength in the Tissues, Arch. Surg. **44**:984 (June) 1942.

3. Bates, R. R.: Absorbability of Catgut, Am. J. Surg. **43**:702, 1939.

4. Bower, J. O.; Burns, J. C., and Mengle, H. A.: The Superiority of Very Fine Catgut in Gastrointestinal Surgery, Am. J. Surg. **47**:20, 1940.

as late as a month or two after operation. These observations have generally been attributed to an abnormal delay in the absorption of the chromic catgut.

It has likewise been observed by many surgeons that clean operative wounds which disrupt within six to ten days may reveal only shreds or fragments or possibly no trace at all of the so-called twenty day chromic catgut originally used in the closure of the wound. This apparently premature absorption has been attributed to various causes. An analysis of the factors entering into abdominal wound disruption with special emphasis on the suture material involved has been previously presented.[5] In an endeavor to obtain a comprehensive view of the ultimate absorption after the loss of tensile strength of the various sorts of surgical gut available, a large number of experimental implants were made in the abdominal muscles of dogs. A limited number of clinical observations were also made from specimens obtained at autopsy or from secondary operations on patients. To facilitate evaluation of the gross condition of the surgical gut in the tissues, the Spalteholz method of preparing cleared tissue specimens was used (this method was also used by Bower, Burns and Mengle [4]). The condition of the catgut was further checked by microscopic sections.

EXPERIMENT

The surgical gut of ten different manufacturers was used in sizes no. 2 to no. 000. This represented essentially the same products as those subjected to the previously reported tests of duration of tensile strength in the tissues and in acid pepsin. Each dog was anesthetized with ether, and the abdomen was prepared for operation by shaving and painting with tincture of iodine. Asepsis was maintained with the aid of sterile towels, split sheets and gowns and gloves as well as face masks and caps for the operators. The instruments were autoclaved, and the knives, the scissors and the tubes of catgut were sterilized by a solution of phenol, which was subsequently washed off with alcohol.

The incision was made in the skin and the subcutaneous tissue, exposing the fascia of the rectus abdominis muscle. The incision was made either lateral or mesial to the part of the rectus muscle in which it was intended to implant the catgut. This was done to avoid any difficulties which might arise because of poor healing of the skin immediately above a catgut implant. The catgut was implanted in the rectus muscle at right angles to the direction of the muscle fibers with the aid of an ordinary curved noncutting needle. After removal of the needle, the free ends were tied by a triple throw square knot. The excess catgut beyond the knot was cut off. It was feasible to have as many as 15 to 25 implants in each of the rectus muscles, depending on the size of the animal. The flap of skin and subcutaneous tissue was then replaced over the line of implants, and the subcutaneous tissue was sutured to the underlying muscular fascia either lateral or mesial to the row of implants, in whichever position it would seal off the implants from the rest of the wound. The skin was then closed with a continuous subcuticular suture of silk reenforced by interrupted sutures when necessary.

5. Jenkins, H. P.: A Clinical Study of Catgut in Relation to Abdominal Wound Disruption, Surg., Gynec. & Obst. **64**:648, 1937.

A varied combination of the different sorts of surgical gut was used in these experimental animals to obtain as much diversification as possible as well as to obtain controlled observations. To permit subsequent identification of the sutures used, it was customary to adopt a certain standard sequence of implantation from upper to lower portions of the rectus muscle. The different sizes from no. 2 to no. 000 of any particular type of catgut were implanted from above downward. The twenty day type of chromic catgut was implanted above the forty day type. Products of different companies placed in the same animal were implanted from the upper to the lower part of the abdomen in the sequence of company 1, company 2 and so on.

In most instances, several sets of implants were made in different animals from the same tubes of surgical gut. In one series of animals, a set of implants was made in one rectus muscle and then at a subsequent date, usually twenty days later, another set of implants from the same tubes of gut used previously were implanted in the other rectus muscle. Whenever catgut was carried over from one operation to another at a later date, it was kept sterile by sealing in individual glass tubes in 95 per cent alcohol. In some instances, implants of the boilable variety of surgical gut were compared with implants of the nonboilable type of surgical gut of the same company. Most of the implants, however, were made with nonboilable surgical gut.

The animals were permitted to survive for varying lengths of time up to a year or more. Usually, they were killed by electrocution. The abdominal wall was then excised after removal of the overlying skin. In a few instances, the animals were reoperated on; the rectus muscles were excised, and the abdomen was closed. The specimens were fixed in 10 per cent solution of formaldehyde for at least twenty-four hours. The tissues were then bleached in a cold solution of hydrogen peroxide, which was sealed and exposed to sunlight for at least one or two days. Less adequate bleaching was obtained by exposure to artificial light. The specimens were then dehydrated by numerous washes in alcohol for several days. At least two washes in absolute alcohol were usually necessary for adequate dehydration. The tissues were then soaked in benzene for twenty-four hours and finally immersed in methyl salicylate. At this stage, a large number of air bubbles usually became apparent in the specimen and obscured the transparency of the tissues. The bubbles were removed by the aid of a suction pump.

If the bleaching and the dehydration were adequate, a clear yellow or orange transparent tissue specimen was obtained in which the chromic catgut implants could be readily identified if present. Plain catgut could not be readily identified in the tissues by this method except in a few instances. Also, it was difficult to identify one brand of twenty day and forty day tanned catgut in the tissues because it had the general appearance of plain catgut.

An opal glass plate was put behind the specimen, and with the aid of illuminated boxes, the gross condition of the various chromic catgut implants could be studied carefully. The condition of the catgut from the standpoint of its gross appearance was classified on the basis of 10 as follows:

10—Intact; no evidence of absorption.

9—Ply unraveling but catgut loop and knot intact.

8—Knot untied spontaneously but catgut otherwise intact.

7—Slight fraying of catgut.

6—Break in continuity of catgut.

5—Moderate or marked fraying of catgut with or without break.

4—Catgut gone except for knot.

3—Fragments of catgut remaining.

2—Shreds of catgut remaining.

1—Trace of catgut remaining.

0—Completely gone.

After the gross condition of the catgut was studied, most of the specimens were photographed for a permanent record. In numerous instances, a small block of tissue was cut out for microscopic sections. It was necessary to wash out the methyl salicylate with several changes of benzene. Then the benzene was removed with several changes of absolute alcohol. The block was then ready to be started on the routine preparation for celloidin (pyroxylin) embedding and subsequent cutting for microscopic sections. A number of microscopic sections were also made of the tissues in which catgut was implanted for the tests of duration of tensile strength previously reported.

By this method, 100 experimental specimens were prepared in which approximately 2,000 catgut implants had been placed. In addition, 35 specimens were prepared from clinical material obtained at autopsy or secondary operation. The general behavior of the various sorts of chromic catgut which were implanted in the tissues can be ascertained by reviewing the photographs of the cleared tissue specimens representing different periods of tissue absorption. In addition to the gross appearance in the tissue of the chromic catgut implants, the microscopic studies of the condition of the catgut and the reaction of the tissues about it provide a number of observations of considerable interest.

The designation of the various brands of catgut as those of company 1, company 2 and so on is purely arbitrary. The method of labeling the catgut as twenty day chromic or forty day chromic is used in this presentation although attention is drawn to the nomenclature of catgut which has been officially approved by the Committee of Revision of the United States Pharmacopeia:

U. S. P. Terminology	Terminology Formerly in Use
Type A—Plain surgical gut (untreated)	Plain catgut
Type B—Mild chromic surgical gut (mild treatment)	Ten day chromic catgut
Type C—Medium chromic surgical gut (medium treatment)	Twenty day chromic catgut; medium hard chromic catgut, ten to twenty day
Type D—Extra chromic surgical gut (prolonged treatment)	Forty day chromic catgut; extra hard chromic catgut, thirty to forty day

RESULTS

A number of variable aspects of the absorption of surgical gut were encountered. There was often an appreciable variation in the rate of absorption of surgical gut in the different experimental and clinical specimens examined. Although the magnitude of variation was considerable in some instances, nevertheless, the large number of specimens available for study permitted reasonably accurate observations on the relative rate of absorption and the average length of time required for complete absorption of the different sorts of surgical gut.

In regard to the relative differences in the rate of absorption, it was found that the smaller sizes of chromic catgut of some of the companies were absorbed more slowly than larger sizes (fig. 2). In other products the rate of absorption of the various sizes was more or less uniform (figs. 1 and 3), although in still other products the smaller sizes were more rapidly absorbed than larger sizes (fig. 4, companies 3 and 5). Exceptions were observed in regard to the various sizes of catgut which were inconsistent with any of the three general trends of behavior already mentioned. The differences in the rate of absorption of the chromic catgut of the various companies was of a greater magnitude than was observed between the twenty day and the forty day chromic catgut (types C and D) of any one company (fig. 4).

The behavior of any particular size, type or brand of catgut from any individual lot was usually fairly consistent, although instances of

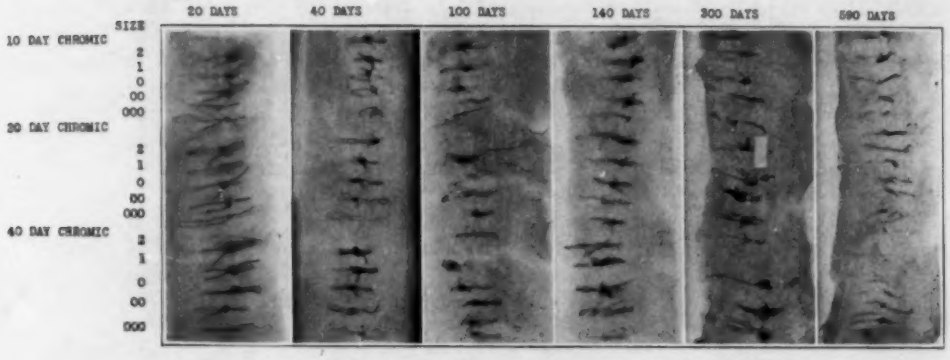

Fig. 1.—Photographs of cleared muscle specimens showing the gross appearance of chromic catgut (company 1) implants in the tissues (series 1937). At the end of twenty or forty days there appears to be no conspicuous evidence of absorption of the chromic catgut regardless of whether the ten day, the twenty day or the forty day type (now called types B, C and D, respectively) was used. Specimens of sixty and eighty days' duration, which are not shown here, did not differ appreciably in their gross appearance from the forty day specimen. The one hundred day specimen shows evidence of beginning absorption, which is fairly well advanced in the one hundred and forty day specimen, as evidenced by the blurred outline of catgut implants. Photomicrographs of the catgut at about this stage of absorption show that the gross appearance is somewhat misleading as far as judging the amount of catgut which remains unabsorbed, because at this stage the catgut has been broken up by the phagocytic cellular response. During this stage, the fragments of the chromic catgut become engulfed in the phagocytic cells, and as the fragments are destroyed, the cytoplasm of the cells apparently takes on the dark green or brown color of the collagen chromate. Dense accumulations of these cells will therefore give a gross appearance which simulates an undigested portion of chromic catgut. In the five hundred and ninety day specimen there still persists some evidence of the chromic catgut implants, but these are residual accumulations of chromic-stained phagocytic cells.

appreciable variation were observed in the surgical gut from identically labeled lots obtained from time to time from the same company. (The term "lot" refers to a sealed box of surgical gut bearing the serial number characteristic of the particular company.)

The absorption of surgical gut from the gross morphologic standpoint was generally classified as rapid or slow. In addition an intermediately absorbed category was sometimes distinguished.

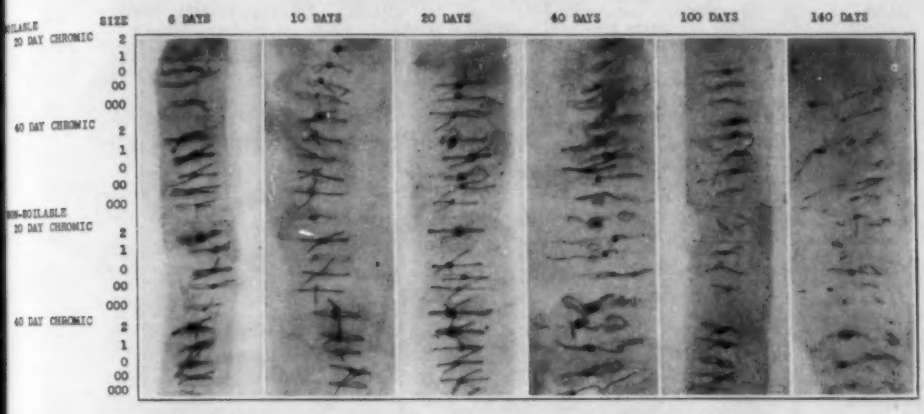

Fig. 2.—Photographs of cleared muscle specimens showing the gross appearance of chromic catgut (company 2) implants in the tissues (series 1937). In the six day specimen it will be observed that all the implants are intact except two. The no. 1 size of twenty day chromic catgut has been practically completely absorbed. The no. 2 size of twenty day chromic catgut has been absorbed except for the knot. In the ten day specimen, most of the implants are to be found intact except as follows: The no. 2 size of twenty day chromic catgut in the boilable series is completely absorbed. The no. 1 size, which is adjacent, is absorbed except for the knot. In the nonboilable series the no. 2 size of the twenty day chromic catgut is absorbed except for fragments of the knot. The no. 0 size of twenty day chromic catgut shows evidence of considerable absorption. In the twenty day specimen, the no. 2 and no. 1 sizes of twenty day boilable chromic catgut are completely absorbed. The no. 2 and no. 0 sizes of forty day chromic catgut are showing some evidence of absorption. In the nonboilable series, the no. 1 size of twenty day chromic catgut is completely absorbed. A tendency for the plies to separate can be detected in the no. 2 size of forty day chromic catgut although the implant is intact. In the forty day specimen there is evidence of considerable absorption. In the one hundred day specimen, the catgut has apparently been less rapidly acted on by the tissues than the forty day specimen would lead one to presume. The no. 2 and no. 1 sizes of twenty day chromic catgut of both the boilable and the nonboilable series have been completely absorbed. The other implants are in a beginning or a moderately advanced stage of absorption which is comparable to some extent to that observed for the catgut of company 1. In the one hundred and forty day specimen, it is difficult to identify the various implants accurately. A fairly advanced stage of absorption is obviously present. Microscopic sections of the one hundred and twenty day specimen show that the catgut has not as yet been broken up to any marked degree by the phagocytic cells.

Most brands of plain catgut were considered as representing rapidly absorbed suture material. In certain chromic catgut products, advanced stages of absorption were observed within ten days, although the catgut was labeled twenty day chromic (fig. 2). Complete absorption of this variety of what was termed rapidly absorbed catgut was usually accomplished within one to three weeks (figs. 8 and 9).

Any particular chromic catgut which could be demonstrated to be intact and free from gross evidence of absorption beyond ten days was usually not completely absorbed for a long time. This constituted the slowly absorbed variety of catgut. The length of time required for complete absorption was generally between three and six months and in some instances longer (figs. 1, 2, 3 and 5). Although in the gross specimens there appeared to be evidence of unabsorbed chromic catgut

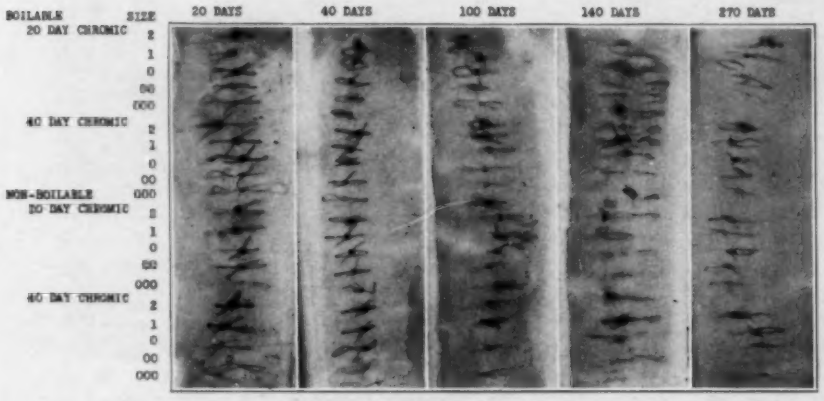

Fig. 3.—Photomicrographs of cleared muscle specimens showing the gross appearance of chromic catgut (company 4) implants in the tissues (series 1937). At the end of twenty days, the implants appear to be relatively intact throughout except for the no. 000 size of twenty day chromic catgut of the nonboilable series. This is almost completely absorbed. The no. 00 size of forty day chromic catgut in this group appears to have untied spontaneously, and there seems to be a break in the continuity of some of the no. 000 sizes of chromic catgut. In the forty day specimen there is little general change from that observed in the twenty day specimen. Two of the no. 000 size sutures and 1 of the no. 00 sizes appear to be fairly well absorbed. In the one hundred day specimen there is evidence generally of beginning break-up of the catgut. The smaller sizes are definitely less conspicuous than the larger sizes, and the latter show a blurring of the outline of the catgut. In the one hundred and forty day specimen, the catgut implants show a rather uniformly advanced stage of absorption which is characterized histologically by fragmentation and destruction of the catgut by the phagocytic cells. In the two hundred and seventy day specimen, the apparent persistence of the chromic catgut implants is due to residual accumulations of chromic-stained phagocytic cells.

for considerably longer than six months, this observation was usually due to a chromic-colored staining in the tissues in the location of the

Fig. 4.—Photographs of cleared muscle specimens showing the gross appearance of chromic catgut implants after twenty days in the tissues (series 1939-1940, dog 792). The sutures of company 1 are all intact. The no. 2 size of the twenty day and the forty day chromic catgut of company 2 shows evidence of some disintegration. The no. 000 size of company 3 appears to be completely absorbed; the no. 0 size, moderately absorbed, and the no. 2 size, beginning absorption. The no. 2 and the no. 000 sizes of the twenty day chromic catgut of company 4 are almost completely absorbed, while the no. 0 size is relatively intact; the forty day chromic catgut is moderately absorbed. The no. 000 size of the chromic catgut of company 5 is completely absorbed, although the larger sizes show little evidence of absorption. The smaller sizes of chromic catgut of companies 3 and 5 are fairly rapidly absorbed. The larger sizes of company 2 are more rapidly absorbed than the smaller sizes. The sutures of company 1 have fairly uniform absorption; those of company 4 have rather inconsistent absorption.

Fig. 5.—Photographs of cleared muscle specimens showing the gross appearance of chromic catgut implants after one hundred days in the tissues (series 1939-1940, dog 727). A moderate amount of the suture material of company 1 appears to be present; a less conspicuous amount of the suture material of company 2 is left, and only a trace of the suture material of company 3 remains. The no. 0 size of the twenty day chromic catgut of company 4 and all sizes of the forty day chromic catgut of company 4 show up fairly well. The no. 2 size of the forty day chromic catgut of company 5 appears to be the best preserved suture of the series; the no. 2 and the no. 0 sizes of the twenty day and the no. 0 size of the forty day chromic catgut of company 5 show up fairly well. (Microscopic sections show moderate or slight evidence of absorption comparable to that shown in the photomicrographs in figure 13.)

implant rather than to chromic catgut which had not been absorbed (figs. 1, 3 and 6). This point will be discussed further in connection with the microscopic studies.

The intermediately absorbed variety of catgut was not necessarily a clearcut entity but appeared to represent a variety of surgical gut which remained intact for about ten days and underwent complete absorption within approximately three weeks to three months. Some of the plain catgut which was studied during the course of this work on the absorption of surgical gut was considered as intermediately absorbed catgut. Also, certain sizes of several brands of chromic catgut appeared to fall within this classification. In some instances, this relatively slowly absorbed or intermediately absorbed variety of surgical gut

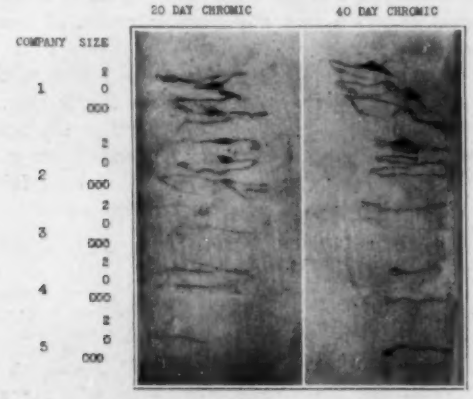

Fig. 6.—Photographs of cleared muscle specimens showing the gross appearance of chromic catgut implants after one year in the tissues (series 1939-1940, dog 791). The suture materials of companies 1 and 2 appear to be present. There are faint traces of the suture material of company 3; there is slightly more evidence of a trace of the suture material of company 4. There is a faint trace of the twenty day chromic catgut of company 5; size 2 of the forty day chromic catgut is noticeable. (Microscopic sections show only clusters of macrophages comparable to those demonstrated in figure 14.)

underwent a rate of absorption comparable to that observed for the rapidly absorbed type of catgut.

From the standpoint of microscopic studies, the absorption of surgical gut was divided into two phases of cellular response on the part of the tissues. The first phase was characterized by a polymorphonuclear leukocytic invasion about the catgut—plain catgut of most varieties (fig. 7) and chromic catgut of certain types (figs. 8 and 9) usually underwent absorption with this kind of cellular response predominating. In this event, the plies of the catgut were invaded, and the catgut was broken up into fragments and shreds by the action of the polymorpho-

nuclear leukocytes. Subsequent to the destruction of the catgut, the cellular response subsided fairly rapidly. Absorption by the leukocytic mechanism was apparently the characteristic aspect of rapid absorption. This was presumably accomplished by a liquefaction of the catgut by enzymes liberated from the leukocytes.

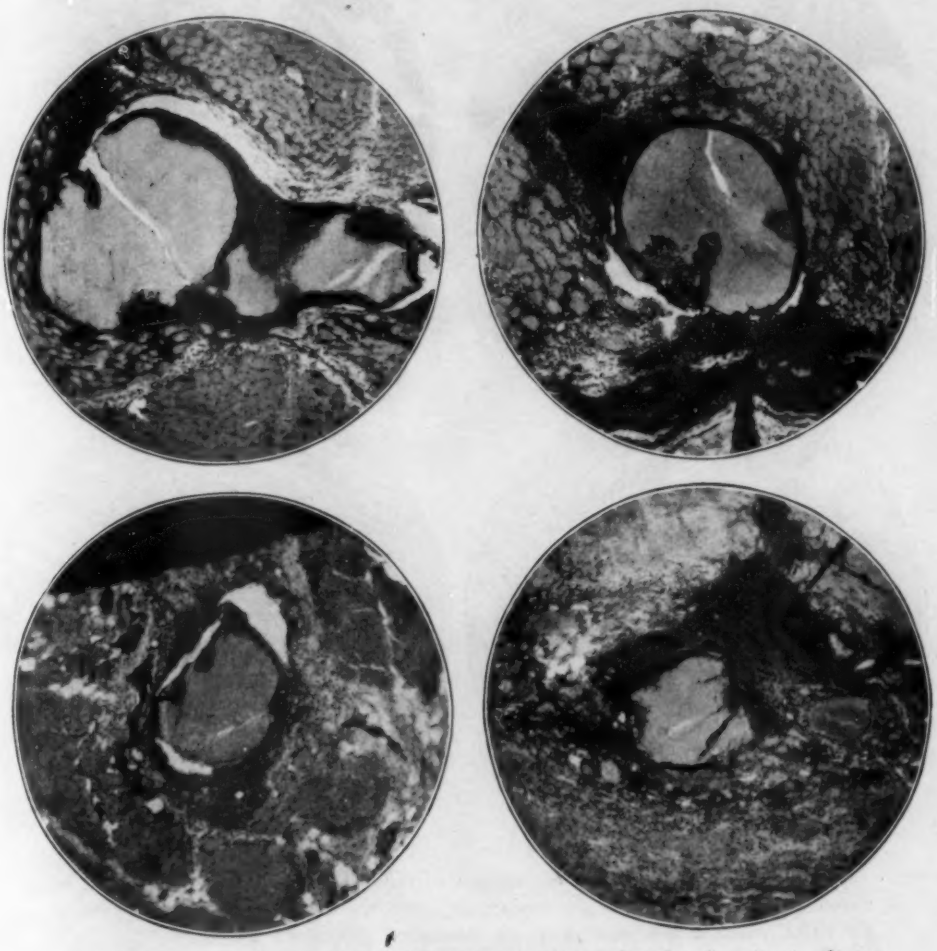

Fig. 7.—Photomicrographs of plain catgut implants after five days in the tissues showing the tissue reaction associated with rapid absorption. There is conspicuous leukocytic response and disintegration of the catgut at this early date evident in all four photomicrographs.

Most varieties of chromic catgut tended to survive the initial polymorphonuclear leukocytic phase. The magnitude of leukocytic response varied considerably in different specimens examined and with certain plain and chromic products. In general, however, most brands of

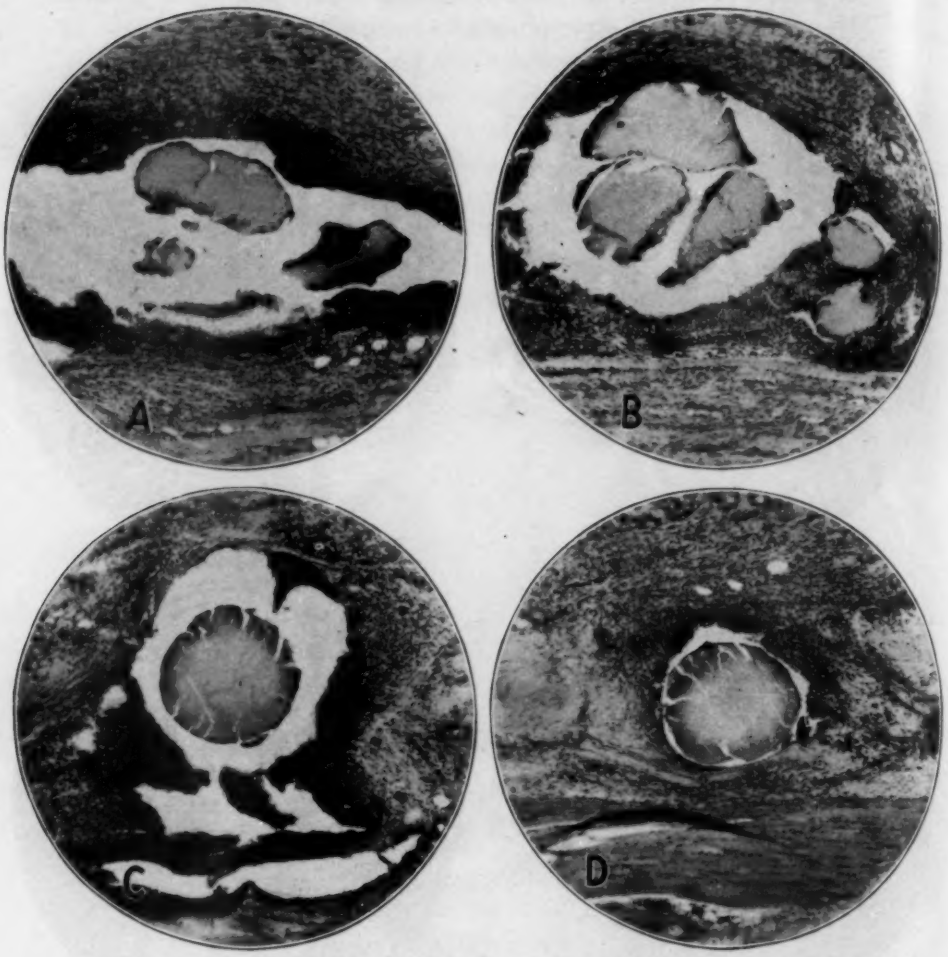

Fig. 8.—Photomicrographs of implants of different sizes of the same brand of chromic catgut (twenty day, company 2) after ten days in the tissues showing the tissue reaction associated with the absorption of chromic catgut.

The conspicuous cellular response seen in these photomicrographs consists mainly of polymorphonuclears, although many macrophages also have accumulated about the catgut. The no. 2 and no. 0 sizes show considerable evidence of disintegration, although the no. 00 and no. 000 sizes appear to be intact. The leukocytic response may subsequently subside, leaving only the macrophages, which have a relatively slow action on the catgut. However, it is probable that the leukocytes will be responsible for most of the absorption of the no. 2 and no. 0 sizes. Whatever is left over from the leukocytic absorptive mechanism will then be taken care of by the macrophages. The conspicuous cellular response demonstrated in these photomicrographs is not necessarily characteristic of most varieties of chromic catgut. *A*, no. 2 size; *B*, no. 0 size; *C*, no. 00 size; *D*, no. 000 size.

chromic catgut appeared to elicit a less intense tissue reaction of a leukocytic type than was usually characteristic for plain catgut or certain types of chromic catgut (figs. 9, 10, 11, 12 and 13). The relatively moderate or slight amount of acute tissue reaction observed for most

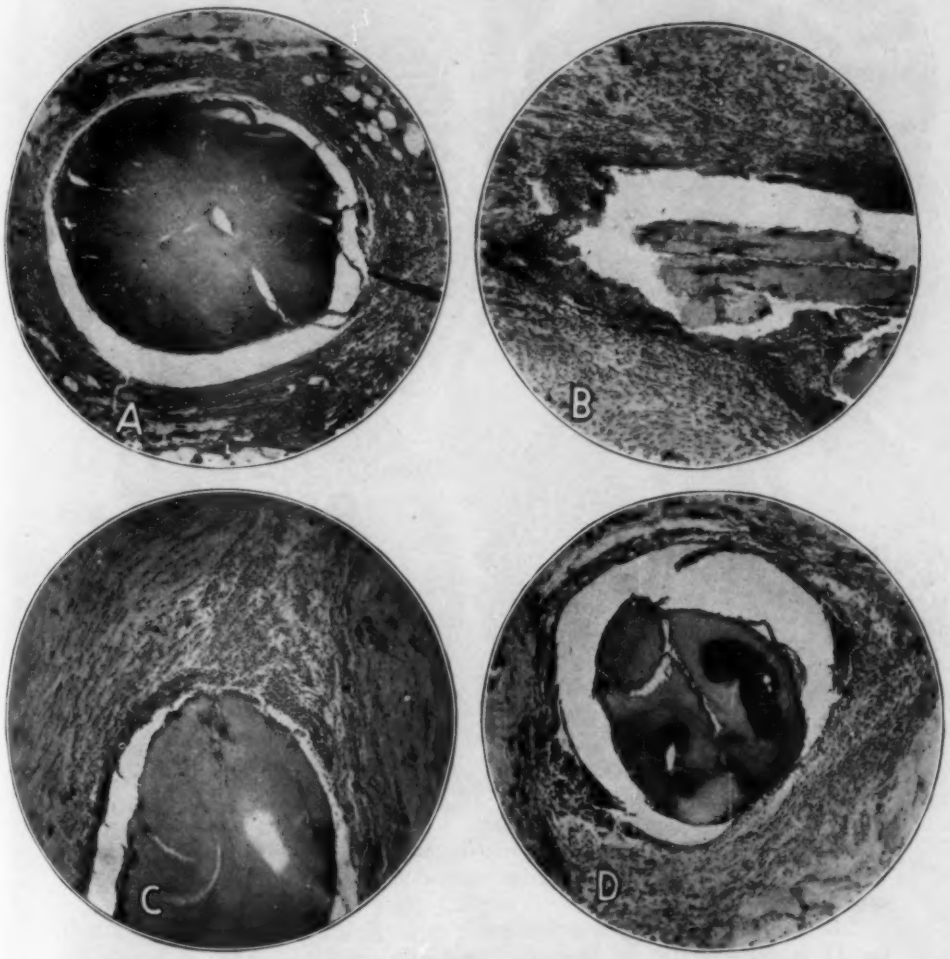

Fig. 9.—Photomicrographs of implants of large size chromic catgut (no. 2) of different brands (twenty day chromic) after ten days in the tissues showing the tissue reaction associated with the absorption of chromic catgut.

In some products (e. g., that of company 2) there is apparently a conspicuous leukocytic response as well as some macrophage response at the end of ten days, although in other products there is relatively slight leukocytic response at this time. Such reaction as does occur appears to be more of a fibroblastic or a macrophage type. The latter response is generally associated with a better state of preservation of the catgut than when leukocytes are present in large numbers. *A*, no. 2 twenty day chromic catgut of company 1; *B*, of company 2; *C*, of company 3; *D*, of company 4.

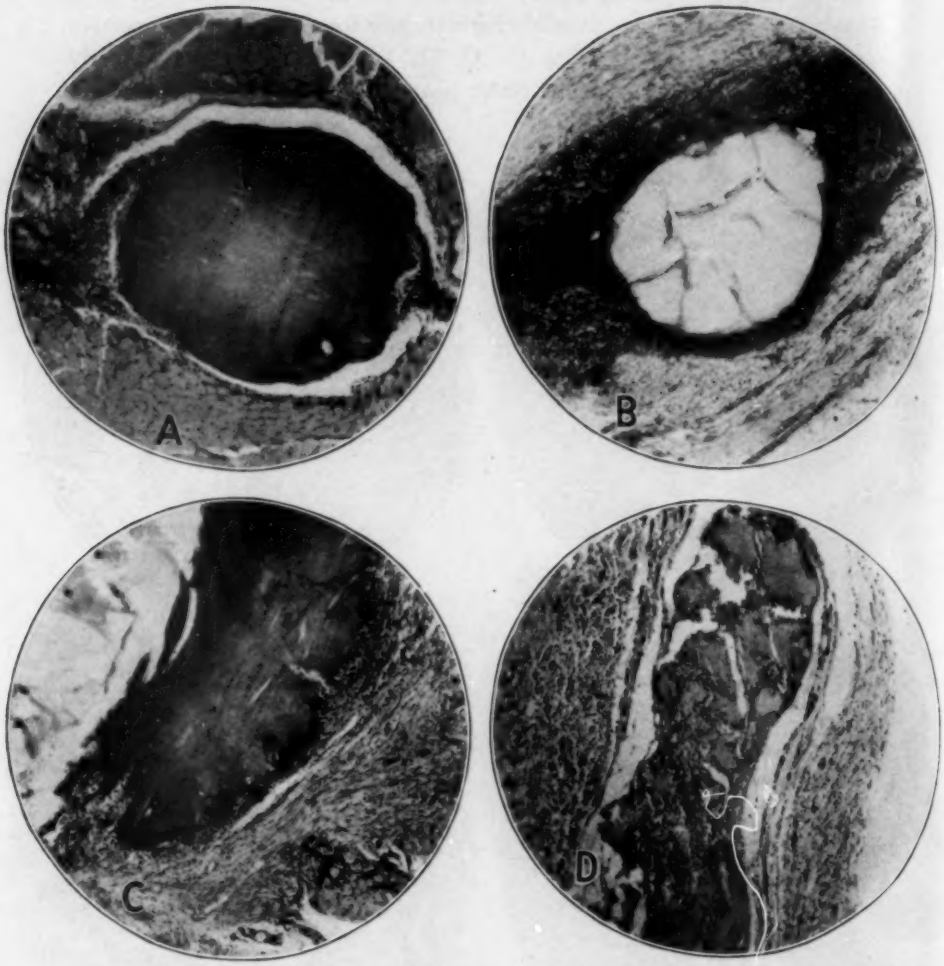

Fig. 10.—Photomicrographs of chromic catgut implants after twenty days in the tissues showing the tissue reaction associated with the absorption of chromic catgut.

The varying tissue response to chromic catgut in the larger sizes (no. 2 and no. 1) is demonstrated by these four photomicrographs of different brands of catgut. The size of the catgut is not per se necessarily the most important factor in the amount of tissue reaction seen, because one may see much more tissue reaction about some of the smaller sizes than will be observed in certain of the larger sizes. Varying stages of absorption of the catgut can be seen. *A*, fibroblastic encapsulation of the catgut and beginning accumulation of macrophages about the periphery. *B*, no apparent evidence of fibroblastic encapsulation; marked leukocytic invasion of tissues about the catgut and early appearance of many macrophages. *C*, irregular areas of absorption along the periphery by macrophages accompanied by scattered lymphocytes and a few polymorphonuclears. *D*, almost complete disintegration of the catgut without evidence of leukocytic response at this time. There is a noticeable fibroblastic response, and occasional macrophages are present.

of the chromic catgut studied constituted a point of considerable importance in this work on the absorption of surgical gut. Aside from the microscopic studies in support of this point there were a large number of gross observations made regarding the amount of exudate character-

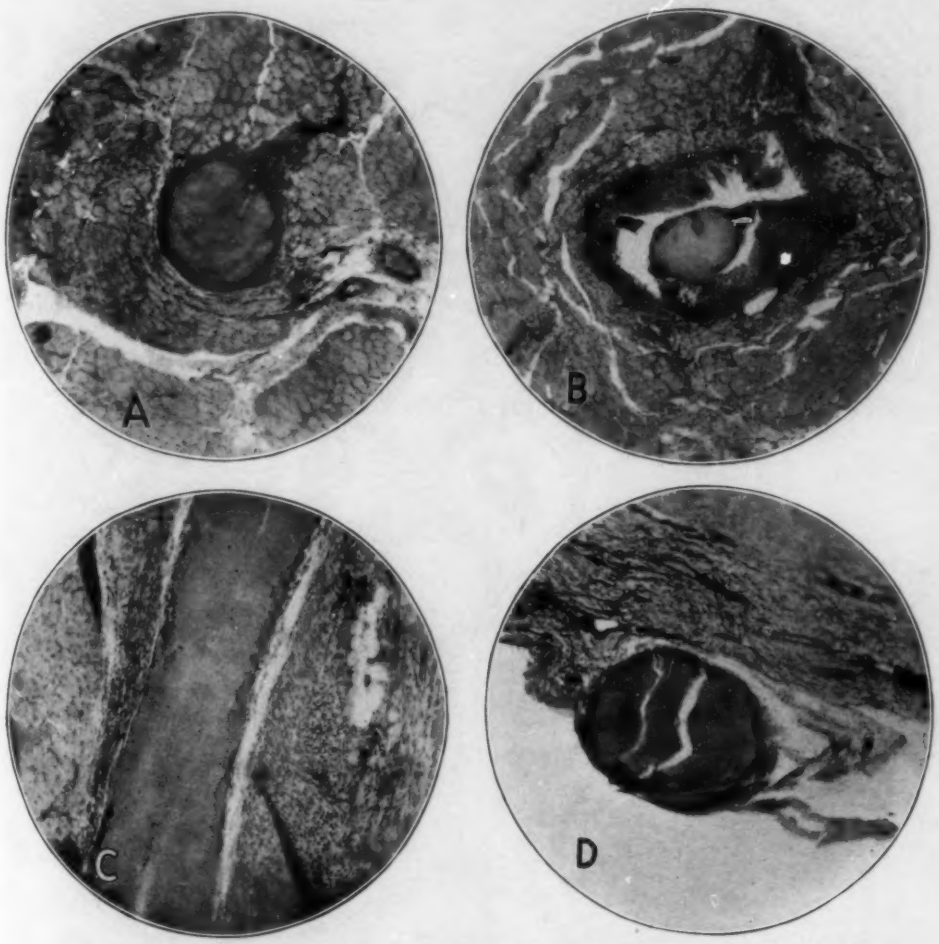

Fig. 11.—Photomicrographs of chromic catgut implants after twenty days in the tissues showing the tissue reaction associated with the absorption of chromic catgut. Absence of appreciable leukocytic reaction in three of the four photomicrographs of different brands of no. 000 size is generally observed for most of the fine sizes of chromic catgut. The conspicuous leukocytic and macrophage reaction seen in one of the photomicrographs is more characteristic of certain products than of chromic catgut in general. *A*, (company 1) moderate fibroblastic response and some macrophages; *B*, (company 2) marked leukocytic and macrophage reaction; *C*, (company 4) relatively slight fibroblastic and macrophage reaction and occasional lymphocytes; *D*, (company 5) relatively slight fibroblastic and macrophage reaction.

istic of the various sizes, types and brands of catgut implanted in the tissues. These observations were made during the course of tensile strength tests previously reported [1] and corresponded with what was observed microscopically.

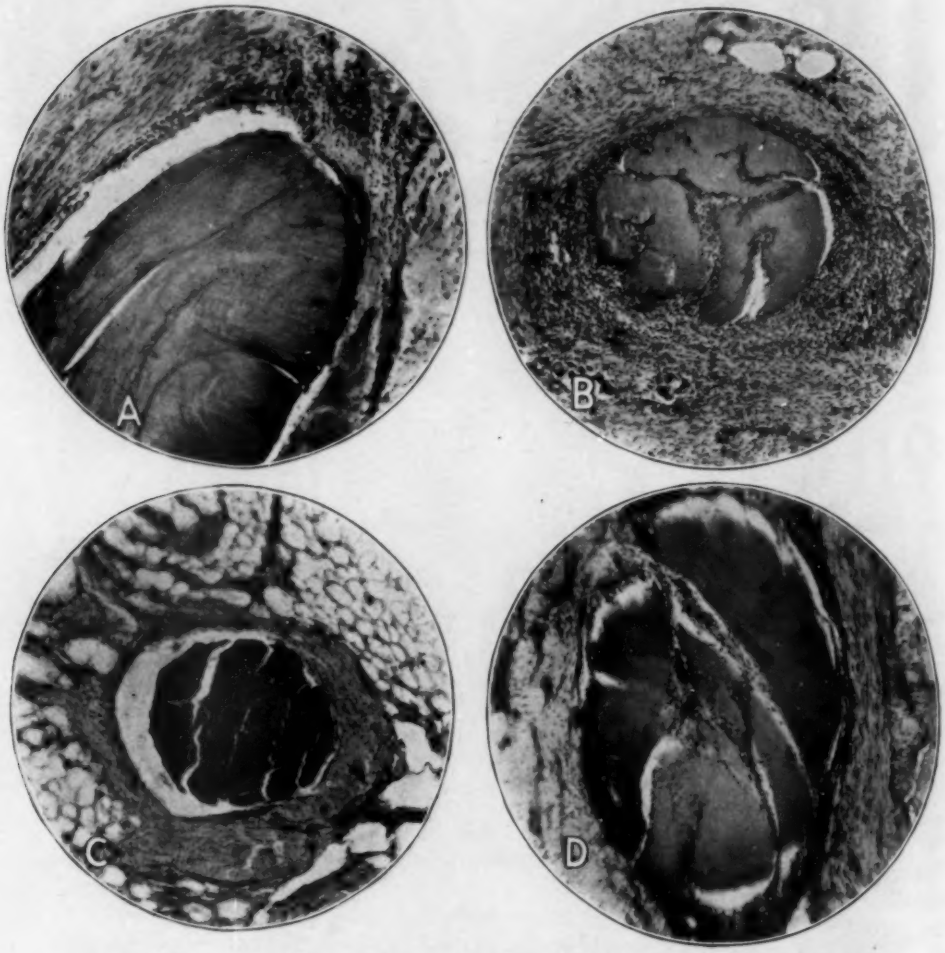

Fig. 12.—Photomicrographs of chromic catgut (no. 0) recovered from patients (at autopsy or reoperation) showing varying amounts of the tissue reaction which is generally observed during the course of slow absorption. *A* (sixteen days), there has been minimal tissue reaction with a few lymphocytes and macrophages; the catgut is intact. *B* (thirty-five days), there has been invasion of the plies of the catgut by macrophages and few lymphocytes; some giant cells are present. *C* (thirty-six days), the cellular response is negligible except for fibroblasts; the catgut is intact. *D* (forty-five days), invasion of the plies of catgut by few macrophages, lymphocytes and fibroblasts has occurred.

The second phase of surgical gut absorption was characterized by the phagocytic activity of macrophages. If the catgut survived the leukocytic phase, the various cell types generally classified as macrophages or histiocytes accumulated about the catgut. The onset of this phase was

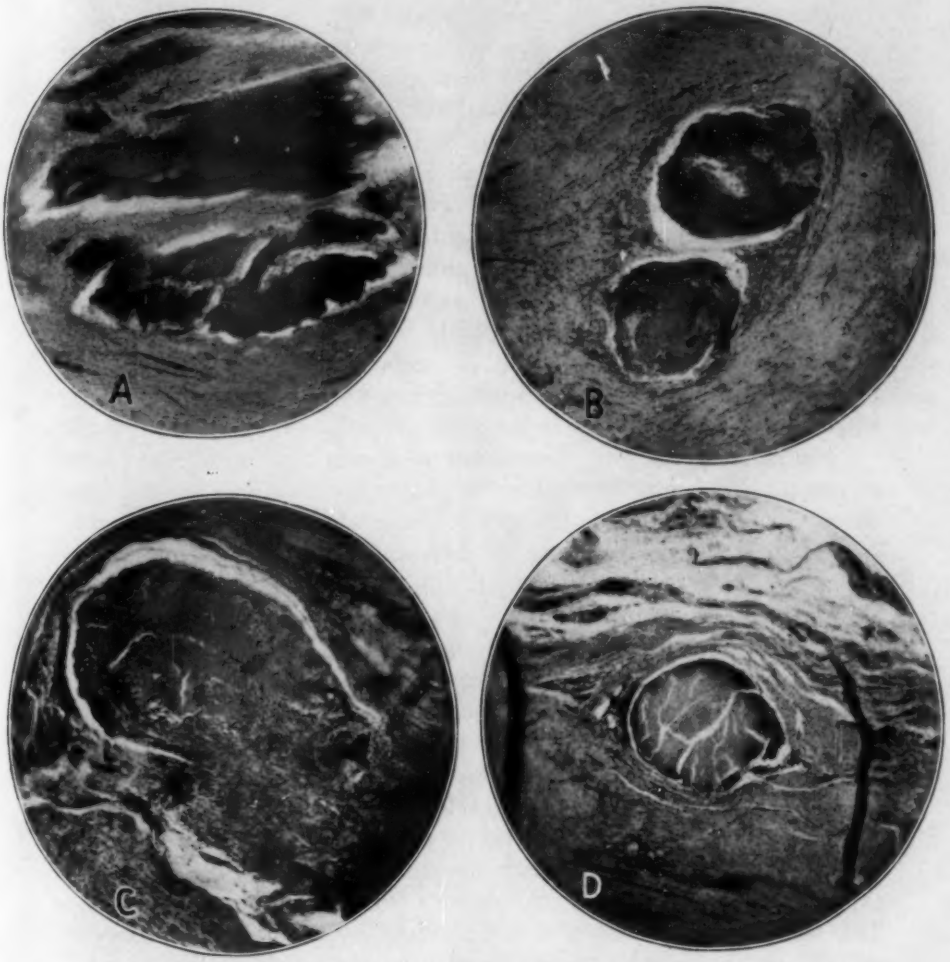

Fig. 13.—Photomicrographs of chromic catgut after three months in the tissues showing the tissue reaction associated with the absorption of chromic catgut. *A* (from autopsy), no. 2 chromic catgut with marked fragmentation and relatively slight cellular reaction. *B* (from autopsy), no. 000 with some invasion of catgut by macrophages. *C* (dog), no. 2 with moderate invasion and destruction of catgut by macrophages but no apparent evidence of leukocytic reaction. *D* (dog), no. 000 catgut which is practically intact, although a few macrophages are accumulating and beginning to invade the strand.

observed as early as in seven to ten days (figs. 8 and 9). There was no sharp transition between the initial leukocytic phase and the secondary macrophage phase. In many instances both phases could be detected, but usually one or the other predominated. Occasionally an intervening period of slight cellular response was observed. Varying amounts of lymphocytic invasion were often associated with the macrophage phase (fig. 12) as well as the polymorphonuclear phase (fig. 8). During the course of the absorption, the macrophages invaded the plies of the catgut and caused irregular areas of absorption from within the strand as well as about the periphery (figs. 9, 10, 11, 12 and 13). The catgut was gradually broken up into smaller and smaller fragments as the absorption progressed (fig. 13). The length of time required for complete absorption of chromic catgut by this macrophage mechanism was three to six months or sometimes longer (fig. 14). In some instances, however, the absorption was apparently completed within three weeks to three months, probably because of an appreciable preliminary action by the leukocytes. Foreign body giant cells were often seen, and (figs. 12 and 14) occasionally one was able to detect a minute fragment of chromic catgut in the giant cell (fig. 14).

The most conspicuous observation made was that during the course of the relatively slow absorption the phagocytic cells took on the color characteristic of the chromic catgut. Dense clusters of these chromic-stained macrophages persisted in the location of the chromic catgut implant for long periods of time (fig. 14) after the catgut was actually absorbed and simulated the gross appearance of an unabsorbed fragment of chromic catgut (figs. 1, 3 and 6). This was observed as late as two years in fresh tissue specimens removed at autopsy or operation as well as in the fixed or cleared specimens.

When chromic catgut remained intact for ten days or more in the tissues, it was usually found to be surrounded by a thin fibrous tissue capsule. This was distinctly noticeable when the gross specimens were dissected at autopsy. The skin and the subcutaneous tissue were usually easily separated from the underlying muscular fascia without actually exposing the catgut knots or the free ends of the catgut beyond the knots. This was possible because this thin fibrous capsule sealed off the catgut exposed on the anterior rectus sheath from the overlying loose subcutaneous tissue. Instances in which the more slowly absorbed varieties of chromic catgut underwent relatively rapid absorption appeared to coincide with failure or delay in this encapsulation process. This gross evidence of fibroblastic response was supplemented also by microscopic observations (figs. 9, 10, 11 and 12).

The behavior of the catgut knot during the course of absorption was interesting from several standpoints. During rapid absorption by the leukocytic mechanism, the knot was generally the last part of the suture

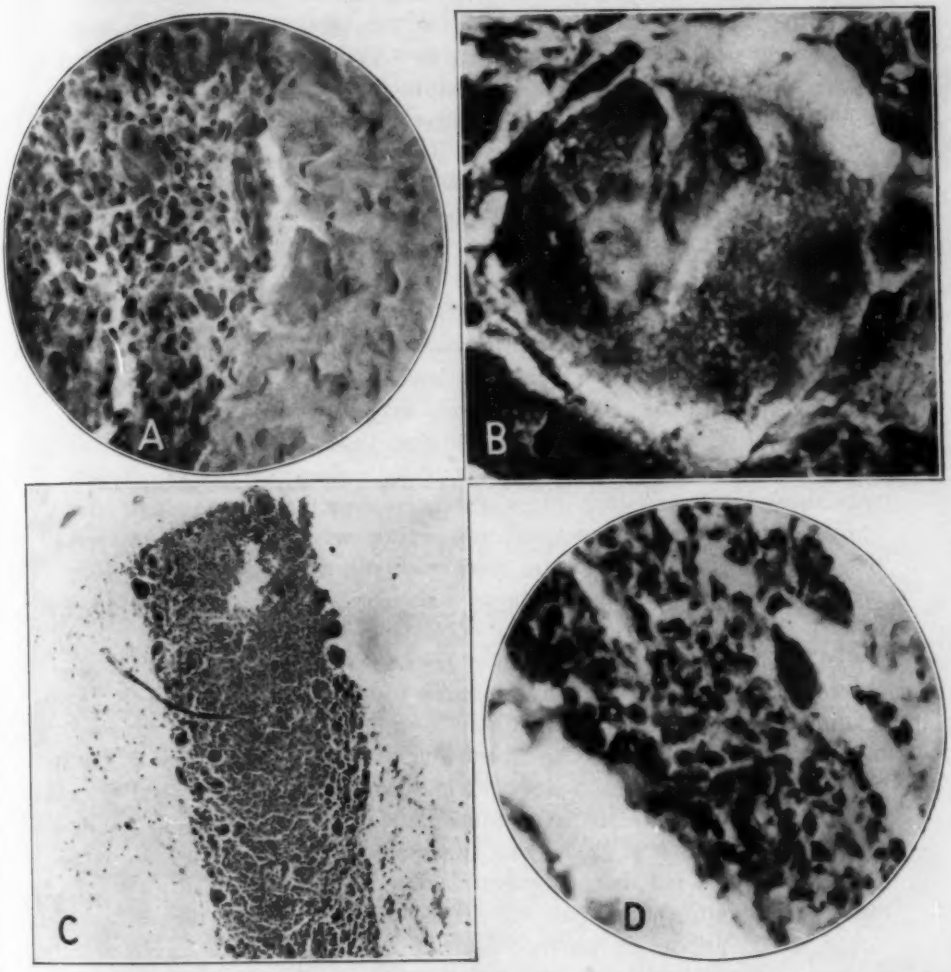

Fig. 14.—Photomicrographs showing the macrophage reaction which persists at the location of the chromic catgut for long periods after the catgut has been absorbed. These dense clusters of macrophages gave a gross appearance which simulated the appearance of an unabsorbed fragment of chromic catgut. No evidence of catgut could be found microscopically, and it appears that the macrophages have taken on the color of the chromic catgut which was absorbed by the macrophages. Occasionally one can detect a minute fragment of chromic catgut within a giant cell; however, this was not observed frequently enough to account for the strain in the tissues which resembled unabsorbed chromic catgut. *A* (six months), macrophage cluster but no evidence of chromic catgut. *B* (thirteen months), large multinucleated giant cell with fragment of chromic catgut engulfed. *C* (seventeen months), macrophages and numerous giant cells. *D* (twenty-seven months), macrophages and occasional giant cells.

to be absorbed (fig. 2). During slow absorption, the knot as a rule underwent absorption at a rate which was more nearly like that of the rest of the suture (figs. 1 and 3). In some specimens, it appeared that the triple throw square knots used for the implants underwent spontaneous untying in the absence of any appreciable evidence of absorption of the catgut (fig. 3). In these experimental implant series there was noticed no tendency to form draining sinuses from the catgut implant to the skin surface.

In certain products, it was not unusual to observe that the plies of the catgut tended to separate rather widely, although there may have been no gross evidence of absorption at that time (fig. 2).

COMMENT

When the slowly or intermediately absorbed type of catgut underwent relatively rapid absorption, this may have been due to several factors. The resistance of the catgut to digestion may have been appreciably less than that of other strands of the same size, type or brand. The tissues in which the catgut was implanted may have responded to the foreign substance with somewhat more exudative reaction than usual; this impaired the fibroblastic encapsulation process which apparently protects the catgut from the leukocytic mechanism of rapid absorption. The presence of some irritating factor of a chemical nature could contribute to such exudative reactions as may occur from time to time.

In the study of pepsin digestion tests, it was pointed out that the chromic catgut of one company appeared to show a somewhat different relation between pepsin digestion and duration of tensile strength in the tissues from that of most other companies. It is rather interesting to point out that this corresponded with the product which appeared from the microscopic studies to have caused a relatively conspicuous acute tissue reaction. It is probable that this more acute tissue reaction, consisting mainly of polymorphonuclear leukocytes, contributed to a more rapid rate of absorption than the degree of resistance of the chromic catgut would appear to warrant in view of the fact that comparable degrees of resistance in other products usually resulted in a slower rate of absorption with considerably less tissue reaction.

The relative differences in the rate of absorption of the various sizes, types and brands of surgical gut corresponded in general with those observed in the previously reported work. However, the duration of tensile strength was not necessarily directly proportional to the time required for complete absorption. The catgut which maintained its tensile strength for less than ten days was usually completely absorbed within a relatively short time after the loss of tensile strength. The catgut which remained intact beyond ten days usually required a long

time for complete absorption. It is not generally realized that the ultimate absorption of the latter type of catgut may require three to six months or sometimes longer. The descriptive literature put out by some of the manufacturers of surgical gut has included statements which do not appear to be confirmed in this work. For example, the twenty day chromic catgut of one manufacturer was stated to maintain its tensile strength for "approximately" twenty days in the tissues and to undergo complete absorption in three additional days. Statements such as this have led to an impression that the normal time required for complete absorption was a matter of several days after the loss of tensile strength instead of the several months observed for a considerable proportion of the twenty day or forty day chromic catgut studied in this work. It may be recalled also that in the observations on the duration of tensile strength in the tissues, it was rather unusual to have twenty day or forty day chromic catgut maintain its tensile strength for a period which would be considered an "approximation" of the absorption time specified on the label.

The behavior of the various sorts of surgical gut in the tissues was apparently related to the fundamental mechanism of absorption. There was on the one hand a polymorphonuclear leukocytic activity associated with rapid absorption, while on the other hand a macrophage activity was associated with slow absorption. In some instances, both types of cellular activity appeared to play a role in what appeared to be intermediate absorption.

There was a considerable difference in the manner in which the cellular response subsided following the completion of absorption. The leukocytic response subsided fairly promptly after rapid absorption. The macrophage response associated with slow absorption or intermediate absorption persisted for long periods after the catgut was actually absorbed (fig. 14).

A point of particular interest was the chromic-colored stain imparted to the protoplasm of the macrophages or histiocytes which participated in the absorption of the chromic catgut. The ability of macrophages or histiocytes to take up various types of vital-staining material in their protoplasm has been generally recognized. However, attention has not been conspicuously drawn to the apparent vital staining of macrophages or histiocytes which have been responsible for the absorption of chromic catgut.

It is probable that most instances in which surgeons have found what appeared to be unabsorbed chromic catgut in a healed incision which was reopened at a secondary operation nine months to two years later can be explained on the basis of persistent clusters of chromic-

stained macrophages.[6] It is exceedingly difficult to distinguish grossly between clusters of chromic-stained macrophages and unabsorbed chromic catgut without a microscopic section.

The character of the cellular response to foreign substances is generally indicative of the absence or the presence of irritating qualities in the foreign substance. Because of the striking differences often observed in the type and the magnitude of cellular response to various sorts of catgut, there are reasonable grounds for presuming that this may represent differences in the extent to which catgut acts as an irritant to the tissues. In view of the frequent observation that most types of chromic catgut were absorbed by a cellular mechanism usually characteristic of relatively nonirritating substances, it is possible that this indicated a nonirritating suture material. The leukocytic response characteristic of plain catgut and certain types of chromic catgut may have indicated an irritating suture material.

Just what contributes to the magnitude or the lack of irritation may differ in various instances. There appeared to be some relation between the resistance of the catgut to digestion as determined by the acid-pepsin digestion test and the magnitude of irritation observed, since the degree of resistance to digestion was generally inversely proportional to the amount of irritation observed. The chromicizing of catgut by the more modern commercial methods beyond some critical point appeared to result in a suture which usually caused less irritation to the tissues than untreated plain catgut. There was no apparent evidence that modern methods of chromicizing superimposed any additional irritating qualities on untreated plain catgut. The extent of chromicizing which accomplished this decreased irritation probably varied. Some methods of chromicizing, which may still be in use, did not appear to accomplish a lessened degree of original irritation, although subsequent to the alleviation of such irritation as originally existed, there was usually a long period of nonirritating and slow or intermediate absorption. Although the relatively resistant chromic catgut, which presumably represented fairly extensive degrees of chromicizing was usually slowly absorbed, this was not necessarily consistently observed. Whether the occasional evidence of irritation and rapid absorption was due to the local conditions of the tissues in which the catgut was implanted or to the presence of an extraneous irritating factor can only be surmised.

Bates [3] also observed that chromic catgut caused less reaction in the tissues than plain catgut. He attributed this to the fact that plain catgut

6. One brand of tanned iodized catgut which has not been available on the market because it was made only to meet the needs of a certain situation was found to be intact as late as three years (Rhoads, J. E.; Hottenstein, H. F., and Hudson, I. F.: The Decline in the Strength of Catgut After Exposure to Living Tissues, Arch. Surg. **34**:377 [March] 1937).

was irritating to the tissues. He found also that the smaller sizes of chromic catgut caused less tissue reaction than the larger sizes and that the smaller sizes remained intact for a longer period than the larger sizes. His observations, however, were limited to the product of one company.

On the other hand, in their work in 1930, Howes and Harvey [7] found that chromic catgut caused a more intense polymorphonuclear and lymphocytic reaction than plain catgut. They observed the proliferation of fibroblasts at the periphery of the chromic catgut after five or six days. The twenty day chromic catgut which they studied at that time was found to undergo complete absorption in nineteen to twenty-three days.

Bower, Burns and Mangle [4] carried out studies on a product which demonstrated the relatively slight tissue reaction of very fine chromic catgut (size no. 00000) as compared with relatively small size chromic catgut (no. 0). It is of interest to note that it is not necessary to resort to such a fine size of chromic catgut as was used in the experiments of these authors to obtain relatively slight tissue reaction with most chromic catgut products. Further, no. 0 chromic catgut of most companies as well as the product which Bowers, Burns and Mangle studied was generally found to be in a better state of preservation at the end of ten days or more than was reported in their work.

Meade and Ochsner,[8] in their study of the relative value of catgut, silk, linen and cotton, found that catgut caused more tissue reaction than the other types of suture material. However, in reviewing the photomicrographs of the cotton, the linen and the silk in their articles in the light of observations made on most of the chromic catgut in our study of suture material, it appears that chromic catgut of certain types does not compare as unfavorably with nonabsorbable suture material from the standpoint of tissue reaction as they were inclined to conclude.

In the work of Bellas and Collins,[9] the tissue reaction of catgut, silk and a new nonreacting, noncapillary suture, known as plastigut, in which the essential components are synthetic plastics (polymerized condensation products of aliphatic and aromatic alcohols with short chain aliphatic aldehydes) was studied. They were impressed with the relatively nonreacting properties of plastigut as compared with catgut

7. Howes, E. L., and Harvey, S. C.: Tissue Response to Catgut Absorption, Silk, and Wound Healing, Internat. J. Med. & Surg. **43**:225, 1930.

8. Meade, W. H., and Ochsner, A.: The Relative Value of Catgut, Silk, Linen and Cotton as Suture Materials, Surgery **7**:485, 1940.

9. Bellas, J. E.: Suture Studies: A New Suture, Arch. Surg. **41**:1414 (Dec.) 1940. Collins, C. U., and Bellas, J. E.: The Influence of Sutures on Operative Wounds, Tr. West. S. A. (1938) **48**:316, 1939.

or even silk. However, their observations on catgut did not apparently include examples of relatively nonreacting chromic catgut such as those found in our work.

Several factors may influence the amount of irritation in the tissues other than such properties as are inherent in untreated surgical gut. Irritating chemicals used in the chromicizing process or unfixed or unstable chromic compounds resulting from the chromicizing process which have not been thoroughly removed from the catgut could possibly explain some of the instances of apparent irritation. The xylene or toluene which has been used as a tubing fluid for boilable catgut is insoluble in water and is difficult to remove completely from the catgut except by thorough washing in alcohol. The presence of xylene or toluene in relatively small amounts in the catgut when it is introduced into the tissues could account for appreciable irritation. The alcohol used in tubing fluid for nonboilable catgut could cause some irritation if it did not evaporate to a considerable extent before the catgut got into the tissues. The presence of chemicals in the tubing fluid designed to act as bactericidal agents also may contribute to tissue irritation. In addition there is some evidence that the alcoholic tubing fluid of some varieties of nonboilable catgut contains appreciable amounts of a liquid which is insoluble in water and which may be the source of irritation if it is carried into the tissues along with the catgut. Further studies on the tubing fluids commonly used will be the subject of a subsequent communication.

In an endeavor to eliminate any possibility of irritation from the tubing fluid or chemical agents therein, it appears logical to consider using surgical gut which has been sealed up in dry tubes after the heat-sterilizing process. When the tube is opened, the dry catgut can be moistened with physiologic solution of sodium chloride to permit whatever flexibility is desired.

Aside from any considerations of the nature of the suture material, the bulk of the suture material involved may appear to contribute to the problem of irritation in the tissues. Although silk is considered to be nonirritating to the tissues, it is generally agreed that the use of large sizes of silk is not desirable for buried sutures because of the incidence of draining sinuses which will occur even in clean wounds. These draining sinuses may be considered evidence of irritation from some points of view, although the fundamental nature of silk is essentially nonirritating in character. The draining sinus represents a failure on the part of the tissues to encapsulate and incorporate the silk because of the bulk involved. In those instances in which the tissue tolerance for a given bulk of fundamentally nonirritating foreign material is

exceeded, one may then expect to find what appears to be evidence of irritation. This is really a matter of the size of the suture material used, rather than of any irritating quality of the suture material.

When draining sinuses develop after the use of large sizes of catgut, it is often attributed to irritating qualities of the catgut, although this explanation may not necessarily be applicable in the light of observations made in this work. The mechanism involved in the formation of draining sinuses from catgut does not appear to differ essentially from that involved in the formation of them from silk, because the type of catgut which is likely to cause a draining sinus is the slowly absorbed, relatively resistant and nonirritating chromic catgut of the larger sizes. The important aspect is that when the bulk of suture material which the tissues will tolerate at any focal point has been exceeded, the draining sinus will develop regardless of whether silk or this variety of catgut is used. The draining sinus represents a failure of the fibroblastic mechanism to encapsulate the foreign material. Although the bulk involved is generally the most important factor in determining the adequacy of the fibroblastic mechanism, other factors, such as bacterial contamination of the wound, unusually large amounts of plain catgut for ligatures, irritating substances from the tubing fluid introduced into the tissues with the catgut or an impaired fibroblastic response of the tissues due to vitamin or nutritional disturbances, may be of significance. It is of interest to note that the type of catgut which causes the most noticeable irritation, as evidenced by the acuity of the tissue reaction, is usually the rapidly absorbed variety of catgut. This kind of catgut would not be present in the tissues long enough to cause a draining sinus.

In view of the fact that some of the so-called twenty day chromic catgut which has been studied was found in advanced stages of absorption in various experimental implant specimens within six to ten days, it is not surprising that surgeons report from time to time that they could find only a few shreds of the chromic catgut which they had used to suture the abdominal wound and which they had an opportunity to examine again in six to ten days because of disruption. It is not necessary to assume an abnormal or premature absorption of the chromic catgut due to peculiarities of the patient's tissues in cases such as this because the rapid rate of absorption may be characteristic for that particular variety of catgut. One can ascertain whether a lot of chromic catgut is of the rapidly absorbed variety by clinical tests, such as the tension suture test or seton test previously described.[5] Also, one can determine whether the digestion time in acid-pepsin solution is more within the range generally found for plain catgut or is substantially more

resistant to digestion than plain catgut.[2] This will give fairly reliable indirect evidence as to whether any particular catgut is of the rapidly absorbed variety.

Not to be overlooked in this study of suture material is the possibility of allergic reactions playing a role in the rate of absorption of the suture materials as well as in the tissue reaction incited. The work of Kraissl, Kesten and Cimiotti,[10] as well as that of Langston [11] and Farris [12] and other workers, must be taken into consideration. In the experimental animals studied in our work there was little likelihood of sensitization to catgut because many of these animals had not had any previous operations. However, the presence of Forssman antibodies of high titer in some of the animals might have been responsible for some differences in tissue reactions. Because of the relative uniformity of reaction incited by the various suture materials in a large series of animals, it is unlikely that allergic phenomena contributed substantially to the tissue reactions described in our work. Pickrell [13] concluded that catgut does not act as an antigen to induce the hypersensitive state.

RECOMMENDATIONS

It is probable that the larger sizes of surgical gut, which are designed for closure of fascial layers of relatively healthy patients by the average surgeon, should have properties comparable to those of what has been described as intermediately absorbed catgut, i. e., about ten days' duration of tensile strength and complete absorption in approximately three weeks to three months. This recommendation is based on an analysis of the situation from several points of view:

1. The minimum time required for the healing of a normal clean wound should be considered approximately ten days. Howes, Sooy and Harvey [14] found that most of the strength of the healing wound was obtained in ten days, although fourteen days was required for maximum strength. Chouke and Whitehead [15] found good healing in eleven days and apparently complete repair after sixteen days.

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10. Kraissl, C. J.; Kesten, B. M., and Cimiotti, J. G.: The Relation of Catgut Sensitivity to Wound Healing, Surg., Gynec. & Obst. **66**:628, 1938.

11. Langston, H. T.: The Problem of Catgut Sensitivity and Its Relationship to Wound Healing, Ann. Surg. **113**:1117, 1941.

12. Farris, J. M.: Tissue Reactions to Suture Materials, Ann. Surg. **114**:1128, 1941.

13. Pickrell, K. L.: Studies on Hypersensitivity to Catgut as a Factor in Wound Disruption, Bull. Johns Hopkins Hosp. **64**:195, 1939.

14. Howes, E. L.; Sooy, J. W., and Harvey, S. C.: The Healing of Wounds as Determined by Their Tensile Strength, J. A. M. A. **92**:42 (Jan. 5) 1929.

15. Chouke, K. S., and Whitehead, R. W.: Wound Healing, Surgery **9**:194, 1941.

2. If one uses surgical gut which is completely absorbed in less than three weeks, the duration of tensile strength will probably be no longer than five to eight days. This rapidly absorbed type of suture material does not have an adequate duration of holding power in the tissues to insure a safe period of healing for the fascial layers.

3. If one uses surgical gut of the slowly absorbed variety in the larger sizes, one may obtain a considerably longer duration of tensile strength. However, one is likely to encounter draining sinuses from time to time because the bulk of relatively resistant suture material may exceed the tolerance of the tissues for foreign substances of a nonirritating quality.

4. The intermediately absorbed type of suture material offers those who prefer to use the larger sizes of catgut an opportunity to have a reasonably safe duration of holding power of the suture, at least for the average run of reasonably healthy surgical patients. This duration of tensile strength will probably not be adequate for debilitated patients or those who might be expected to have some appreciable delay in wound healing because of vitamin C deficiency or hypoproteinemia. The use of this intermediate type of suture material in the larger sizes does not eliminate the possibility of an occasional draining sinus; however, the incidence of this condition should be expected to be appreciably less than when one uses the larger sizes of slowly absorbed chromic catgut.

The practical application of this study of the absorption of surgical gut from the standpoint of clinical surgery revolves about minimizing the bulk of suture material concentrated at any one point in the operative wound. The logical answer to the problem of wound closure with catgut is the use of the smaller sizes (no. 0, no. 00 and no. 000) of slowly absorbed chromic catgut for suturing fascial layers such as the anterior rectus sheath or the midline fascia (interrupted technic). This will give a maximum duration of holding power of the absorbable type of suture material (with preferably fifteen to twenty-five days' duration of tensile strength) without undue difficulties from draining sinuses because of the relatively small bulk of suture material involved at any one point in the wound.

Because of the relatively acute tissue reaction generally associated with plain catgut, it seems desirable to minimize the total bulk of this rapidly absorbable suture material. The tissues will tolerate moderate amounts of the smaller sizes, especially the no. 00 and no. 000 sizes, without appreciable clinical evidence of reaction or exudation. Considerable amounts of the larger sizes (no. 2 and no. 1) of plain catgut may contribute to the reaction and the exudation which are generally described as "characteristic of catgut wounds" by those who advocate nonabsorbable suture material. It is relatively infrequent that a situation is encountered which requires a plain catgut of greater tensile strength

for ligatures in the superficial tissues than is afforded by a no. 00 size (7 pounds [3.2 Kg.]) or at most a no. 0 size (10 pounds [4.5 Kg.]).

In a clinical trial of fine chromic catgut of the slowly absorbed type for ligatures (no. 000) in the superficial tissues, it was not found entirely satisfactory because it was occasionally necessary to remove fragments, usually knots, of the chromic catgut at somewhat later dates. If one has occasion to ligate a vessel of appreciable size in the superficial tissues, however, it is safer to use fine chromic catgut than fine plain catgut. The latter may become so softened by the tissue fluids that it may untie spontaneously before the vessel becomes securely occluded from an organized clot. Taylor [16] found that plain catgut which has been moistened is not a satisfactory material with which to obtain a secure knot as compared with other types of suture material, regardless of the type of knot used. Ligatures of fine chromic catgut appear to be better tolerated in muscle or on muscular fascia than in the subcutaneous tissues.

Relatively fine chromic catgut offers a more reliable closure of the peritoneum than is afforded by larger sizes of plain catgut. Howes and Harvey [17] drew attention to the fallacy of using a suture which has a tensile strength far in excess of the holding power of the tissues in which it is inserted. Their extensive work on suture material and wound healing brought out the importance of the surgical principle of using smaller sizes of catgut for wound closure. Their recommendations for the size of suture and ligature material based on their work have been largely responsible for the wider use of the smaller sizes of catgut. The recommendations presented by us in the preceding paragraphs regarding the selection of the smaller sizes of catgut for interrupted technic are essentially a reflection of their views on the subject, supported and extended by data derived from our own study.

One is hesitant, however, to make any specific suggestions which might lead to the use of suture material with which the user is unaccustomed until such time as the various manufacturers are somewhat more in accord regarding the absorptive qualities of the various sizes and types of chromic catgut. The use of the smaller sizes (no. 0, no. 00 and no. 000) of chromic catgut from some sources could lead to serious consequences if it should prove to be a product which is more rapidly absorbed in the smaller sizes. Nevertheless, the fundamental points

16. Taylor, F. W.: Surgical Knots, Ann. Surg. **107**:458, 1938; Surgical Knots and Sutures, Surgery **5**:498, 1939.

17. Howes, E. L.: The Immediate Strength of the Sutured Wound, Surgery **7**:24, 1940. Howes, E. L., and Harvey, S. C.: The Strength of the Healing Wound in Relation to the Holding Strength of the Catgut Suture, New England J. Med. **200**:1285, 1929. Howes, E. L.: How to Use Catgut, Surg., Gynec. & Obst. **73**:319, 1941.

derived from this study of the absorption of surgical gut lead one to recommend the use of the smaller sizes of catgut if properly labeled regarding their absorptive qualities.

SUMMARY

Experimental and clinical observations were made on the absorption time in the tissues of approximately 2,000 or more catgut implants.

The relative rate of absorption of the various sizes, types and brands of surgical gut corresponded in general with previous observations on the duration of tensile strength in the tissues and the digestion time in acid-pepsin solution.

The length of time required for complete absorption after the loss of tensile strength was as follows: The catgut which usually lost its tensile strength in less than ten days was rapidly absorbed within one to three weeks. The catgut which usually maintained its tensile strength beyond ten days was generally slowly absorbed within three to six months. Catgut which remained intact for about ten days was often intermediately absorbed between three weeks and three months.

The mechanism of absorption presented certain fundamental differences in that a polymorphonuclear leukocytic activity was usually associated with rapid absorption, while a macrophage activity was generally the conspicuous aspect of slow absorption. A leukocytic response of varying magnitude was present as a preliminary phase of slow absorption; however, it was usually not conspicuous and did not appear to contribute noticeably to the absorption. In intermediate absorption, both types of cellular mechanisms probably contributed to the process of absorption.

Following rapid absorption by the leukocytic mechanism, the cellular response subsided promptly. However, after the completion of slow absorption or intermediate absorption, the macrophages or histiocytes often remained in the tissues for a long time.

The macrophages or histiocytes which participated in the absorption of chromic catgut appeared to take on the color characteristic of the particular catgut.

The presence of persistent clusters of chromic-stained macrophages or histiocytes in the tissues often simulated the gross appearance of unabsorbed chromic catgut.

Most varieties of chromic catgut elicited less tissue reaction of a leukocytic or exudative type than plain catgut.

CONCLUSIONS

The method of labeling surgical gut (catgut) which has recently been adopted as a result of the recommendations of the Committee for Revision of the United States Pharmacopeia is a substantial improve-

ment over that formerly used. The fallacy of designating a specific number of days as the absorption time, such as ten days, twenty days or forty days, has been clearly demonstrated.

Although the present adopted classification for labeling surgical gut recognizes four different types, it would appear from this work that there are probably not more than three general categories into which surgical gut can be reasonably classified on the basis of absorptive qualities.

There do not appear to be any major clinical problems in wound closure which cannot be reasonably well solved by absorbable suture material. Excessive tissue reaction, inadequate duration of holding power of the suture and foreign body reactions, as evidenced by draining sinuses, can be prevented to a considerable extent by the proper selection of suture material from the standpoint of size and absorptive qualities.

More uniform absorptive standards for the different types of surgical gut from the various manufacturers would be of considerable aid to the surgeon in selecting the absorbable suture material best suited to his needs.

Dr. William B. Steen, of Tucson, Ariz., gave many helpful suggestions during the preparation of this paper.

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ESSENTIAL BIOCHEMICAL DERANGEMENTS IN HYPERTHYROIDISM

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Exhaustive efforts to find measurable abnormalities of the inorganic constituents, other than of iodine, in the blood of patients with hyperthyroidism have been fruitless. The literature on these endeavors was well summarized by Maddock, Pedersen and Coller [1] and by Bartels.[2] It is not sufficiently appreciated with what care the constancy of concentrations of the electrolytes, particularly of the cations, is maintained. Yet all who have particular interest in this field must have felt the urgency of the belief that something measurable by biochemical methods must be importantly disturbed in patients with thyrotoxicosis and have wished, to quote Maddock, "we only knew what to measure." It is my contention that investigators have been analyzing the wrong body fluid, as will presently be shown.

SERIAL DETERMINATIONS OF THE CARBON DIOXIDE–COMBINING POWER OF PLASMA

My own interest in the acid-base equilibrium of the patient with hyperthyroidism was aroused in 1930 in connection with my development of the breath-holding test.[3] The work of Gesell [4] indicated that the p_H of the respiratory center was the final factor in determining the breaking point, beyond which voluntary apnea was not possible and that tissue acidosis, by whatever means produced, reduced the ability to hold the breath. There was little evidence bearing on the possibility that there might be an acidosis in thyrotoxicosis, for the English and American literature on the subject apparently started and stopped with single observations on the carbon dioxide–combining power of the

Read before the American Association for the Study of Goiter, Boston, May 1941.

1. Maddock, W. G.; Pedersen, S., and Coller, F. A.: Studies of Blood Chemistry in Thyroid Crisis, J. A. M. A. **109**:2130 (Dec. 25) 1937.

2. Bartels, E. C.; Stuart, C. K., and Johnson, E. C.: Tr. Am. A. Study Goiter, 1940, p. 133.

3. Bartlett, W., Jr.: Surg., Gynec. & Obst. **63**:576, 1936.

4. Gesell, A., cited by Bartlett, W., Jr.: Tr. Am. A. Study Goiter, 1930, p. 129.

TABLE 1.—*Basal Metabolic Rate and Carbon Dioxide–Combining Power of the Plasma Before and After Thyroidectomy*

Patient	Age	Sex	Disease	Patient Unstabilized		Before Operation		After Operation	
				Basal Metabolic Rate	Carbon Dioxide-Combining Power of Plasma, Volumes per Cent	Basal Metabolic Rate	Carbon Dioxide-Combining Power of Plasma, Volumes per Cent	Basal Metabolic Rate	Carbon Dioxide-Combining Power of Plasma, Volumes per Cent
1	30	M	Exophthalmic goiter	+91*	50	+32*	60	+ 4	64‡
2	50	F	Exophthalmic goiter	+75 (?)	56	.....	..	+10	56
3	22	M	Exophthalmic goiter	+70 (?)	61	+16	60	+11	59‡
4	39	F	Exophthalmic goiter	+40	55	+37	53†	+ 7	53
5	42	F	Exophthalmic goiter	+80 (?)*	51	+42	52†	+24	59
6	44	F	Exophthalmic goiter	.....	..	+34*	54	+16*	53‡
7	23	F	Exophthalmic goiter	+26	58	+14	62	— 4	65‡
8	29	M	Exophthalmic goiter	+64	60	+23	61	+19	60‡
9	37	F	Exophthalmic goiter	.....	..	+16	57	+ 5	60‡
10	59	F	Toxic adenoma	+32	72	+14	68	+15 (?)	74
11	38	F	Toxic adenoma	.....	..	+22	61	—15	57
12	48	F	Toxic adenoma	.....	..	+25	62	— 9	67
13	36	F	Toxic adenoma	+45	57	....	..	+ 2	67
14	27	F	Toxic adenoma	.....	..	+ 3	61	0	59
15	52	F	Toxic adenoma	.....	..	+31	59	+16	58

* Auricular fibrillation.
† Vena puncture difficult.
‡ Two stage thyroidectomy.

arterial plasma of 6 patients by Davies, Meakins and Sands [5] in 1924. These authors reported values falling within normal limits. A few reports [6] were found in the foreign literature, but there was decided conflict in the results, serial studies during the course of treatment were few, and complicated cases were frequently included. Accordingly, between 1933 and 1935, I made serial determinations of the carbon dioxide–combining power of the venous plasma of 15 patients with thyrotoxicosis and have since added results obtained in 3 additional cases. Observations were made on the patient (1) when unstabilized (usually untreated), (2) when well stabilized and ready for operation and (3) on the fifth to the seventh postoperative day. I did not find values outside the range of normal in any of these determinations or in numerous other single determinations, including one on a patient in spontaneous crisis. On the other hand, it seemed of possible significance that in 8 of these 18 cases, a measurable rise in alkali reserve was observed with clinical improvement and that the sickest patients showed values at the lower limits of normal. Among the remaining patients, no variation beyond the limit of error of the method was observed, except for 1 patient, who showed a small drop in alkali reserve after operation. These data are recorded in table 1.

RESPONSE OF THE CIRCULATION TO MEASURED EXERTION

In the course of these studies, I became interested in the response of the circulation to measured exertion and have reported elsewhere [7] the value of the estimation of the pulse rate and the pulse pressure in the differentiation of mild hyperthyroidism from conditions simulating it. Moreover, the carbon dioxide–combining power of the plasma in the patient with thyrotoxicosis falls sharply after brief light exertion and is slow to return to resting values, while it shows little or no measurable drop after similar exertion in a normal person. It seemed clear, therefore, that the patient with thyrotoxicosis maintained a normal alkali reserve when at rest but that a decided diminution into the range of acidosis developed on exertion. The reasons for this and the possible biochemical derangements accompanying it were not yet clear, and I was not hopeful of finding them in the blood by existing technics. Nor

5. Davies, H. W.; Meakins, J., and Sands, J.: Heart **11**:299, 1924.

6. Walinski, F., and Herzfeld, E.: München. med. Wchnschr. **73**:2153, 1926. Damble, K., and Reuter, A.: Arch. f. klin. Med. **125**:690, 1933. Coelho, E.: Endokrinologie **10**:74, 1932. Altenburger, E., and Boger, A.: Klin. Wchnschr. **12**:1983, 1933. Skold, E.: Arch. f. klin. Chir. **151**:600, 1928. Zondek, H.: Deutsche med. Wchnschr. **55**:345, 1929. Koenig, W.: Arch. f. klin. Chir. **164**:213, 1931.

7. Bartlett, W., Jr.: Endocrinology **22**:543, 1938; J. Mississippi Valley M. Soc. **63**:96, 1941.

TABLE 2.—*Total Titratable Acid of the Urine in Hyperthyroidism*

Patient	Age	Sex	Patient Unstabilized (Admitted)			Before Operation			After Operation (Patient Discharged)		
			Rate	Acid, Cc., Tenth Normal	Basal Metabolic Rate	Days	Acid, Cc., Tenth Normal	Basal Metabolic Rate	Days	Acid, Cc., Tenth Normal	Basal Metabolic Rate
1	52	F	4	270 (334-204)	+28	2	93 (136- 50)	+20	3	85 (122- 62)	
2	44	F	..	.....	....	5	237 (299-153)	+18	3	251 (291-209)	+19
3	48	F	1	180	+38	4	64 (84- 46)	+17	4	18 (51- 0)	+10
4	29	F	7	316 (422-257)	+41	3	247 (263-233)	+15	3	128 (136-111)	+ 4
5	56	F	7	276 (326-207)	+29	3	193 (273-153)	+21			
						3	155 (228-111)	+11	4	126 (163- 68)	+ 4
6	32	F	..	.....	....	..	.....	+38	5	195 (249-142)	+12
									3	92 (90- 94)	
7	17	F	6	382 (455-294)	+38	..	.....	....	5	136 (204- 73)	+ 5
8	60	F	3	314 (348-262)	+36	6	197 (252-100)	+31	5	327 (429-185)	
									4	220 (238-177)	+19
9	19	F	5	357 (388-315)	+50	10	135 (193- 86)	+24			
								+16	6	96 (147- 65)	—13

did the developing interest in impairment of liver function in thyrotoxicosis throw immediate light on this question of fundamental importance.

URINARY EXCRETION OF ACIDS IN HYPERTHYROIDISM

An investigation of the urine seemed to offer more promise than that of any other body fluid, and I recently presented a detailed summary of my findings.[8] At the suggestion of Somogyi, I have studied the total titratable acid of the urine in some 15 hospitalized patients who were given diets, constant, in each case, in the quantities of basic and acid-forming components and in total daily caloric intake. These diets were maintained throughout the preoperative period of hospitalization and were ordinarily resumed on the third or fourth postoperative day. After a preliminary period of stabilization with the diet, daily collection of twenty-four hour urine under standard precautions was carried out and was resumed in the postoperative period until the patient's discharge from the hospital. The period of preoperative observation varied from five days to six weeks; the postoperative studies lasted from three to nine days after the resumption of the diet. The difficulties of maintaining such a regimen are not inconsiderable, but for 9 of the patients the data are complete enough to furnish dependable evidence, and excerpts from the protocols appear in table 2. The number of consecutive days selected in each period of observation, the average excretion of total titratable acid (expressed in terms of cubic centimeters of tenth-normal acid) for this number of days, together with the range of excreted acid during this period are given. Patients 5 to 9, inclusive, were operated on by a two stage procedure; hence data in the second line in each of these cases pertains to the second lobectomy. Physical activity of all patients during the period of observation was limited to getting from bed to chair and to the bathroom.

These results have been discussed at length elsewhere.[8] It is clear that a close relation exists between the clinical course of the patient and the excretion of total titratable acid in the urine. When the improvement has been pronounced in the preoperative period (patients 1, 3 and 9), the fall in quantity of excreted acid has been profound. When the basal metabolism has been promptly reduced postoperatively below admission observations (patients 3, 4, 5, 7 and 9), the last recorded quantities of acid excreted before discharge from the hospital are only one fourth to one seventh of the amounts excreted on admission. On the other hand, when a considerable fall in the basal metabolic rate is not obtained promptly after operation (patients 2 and 8), the postoperative excretion of acid is not importantly different from that of the

8. Bartlett, W., Jr.: Proc. Soc. Exper. Biol. & Med. **45**:196, 1940.

immediately preoperative period, though it has fallen considerably from the amounts excreted on admission.

Patient 9 was followed in more detail over a period of some eight weeks, during which she experienced several minor exacerbations while in a relatively refractory phase of the disease. During such exacerbations, the constituents of her urine under study would vary in characteristic ways, as indicated in table 3 (under the dates of January 27 and 28), in that the total acid, the organic acid and the ammonia would rise and the p_H would fall. I regard the rise of urinary ammonia as an expression of an effort to conserve fixed base under stress. By contrast, the fall in the titrated components and the rise in p_H following the completion of the two stage thyroidectomy was striking. Comparison of the postoperative values for total titratable acid with the

TABLE 3.—*Urinary Findings in Case 9*

	Before Operation				Operation		After Operation			
Date	1/25	1/26	1/27	1/28	2/7	2/29	3/6	3/7	3/8	3/9
Volume	2,100	1,500	2,100	2,650			3,100	2,750	2,350	2,740
Total acid *	142	102	172	190			99	99	65	65
Organic acid †	26.8	14.4	20.1	33.9			35.9	26.4	26.3	21.9
Ammonia nitrogen ‡	0.239	0.211	0.281	0.439			0.558	0.481	0.439	0.446
p_H	6.0	6.0	5.8	5.8			6.5	6.5	...	7.0
Basal metabolic rate	...	...	...	+32			...	...	...	—13

* Tenth normal, cc. per 24 hours.
† Milliequivalents per 24 hours.
‡ Gm. per 24 hours.

quantities excreted on admission (table 2) some ten weeks previously indicates the great change that had taken place.

I have not identified the organic acids the excretion of which varies in the same direction as that of the total titratable acid, but my assumption is that they are ketone acids. The tendency of patients with thyrotoxicosis in postoperative reactions to ketosis seems to be generally known but is not often commented on. Of great significance, I believe, was the recent demonstration by Somogyi [9] of large quantities of ketone acids in the blood of certain patients with hyperthyroidism. In 3 of my own cases, serial determinations of the carbon dioxide-combining power of the plasma showed a rise in alkali reserve coincident with a fall of total titratable urinary acid in 2 cases but insignificant changes in alkali reserve when only a small decrease in urinary acid excretion occurred in the third case. Whether this correlation will be maintained in a significant number of cases remains to be seen.

9. Somogyi, M.: Personal communication to the author.

COMMENT

The significance of these observations on the mechanisms for maintenance of acid-base equilibrium extends beyond the mere demonstration of a state of acidosis, more or less well compensated, as characteristic of thyrotoxicosis and varying with the severity of the disease. I believe that they have an important bearing on the manner in which the tissues take up and release water (and electrolytes). This point has been discussed briefly in a previous paper,[10] in which the hydration of the patient with hyperthyroidism was reviewed. I pointed out that all the known derangements of metabolism in thyrotoxicosis worked toward the retention of water by the tissues in the exacerbations seen spontaneously and after operation ("crisis in miniature"). The occurrence of cerebral and pulmonary edema as characteristic events of crisis, even in patients who showed obvious dehydration, was stressed, and the demonstration by Coller and Maddock [11] of actual gain in weight with fall of insensible perspiration in the period of rising temperature after operation was emphasized. I believe that this has not been given the attention it deserves, for the common clinical practice has been to give large quantities of fluids, often directly into the circulation, at a time when the tissues are already unable properly to handle water. I therefore urged that fluids be restricted in such situations and that hypertonic dextrose be given intravenously to combat the tendency to water retention and to guard against ketosis. The evidence brought forward by Bartels [12] and Brown and McCray [13] of a reduction in plasma proteins in hyperthyroidism was not sufficiently emphasized as an important indication that the patient cannot be properly hydrated until the plasma proteins have been restored to normal. My own unpublished data substantiate these findings and indicate further that a reversal of the albumin-globulin ratio is a common occurrence in the immediately postoperative phase. Pending increase in the colloid osmotic pressure of the blood by transfusion of plasma or of whole blood or by the administration of acacia, limitation of fluids and the use of hypertonic electrolytes intravenously offer an alternative method of preventing serious and often fatal waterlogging of the tissues, especially of the brain and the lungs. The therapeutic use of oxygen in high concentration aids, of course, in the delivery of oxygen to the tissues at higher tension and makes easier the more complete oxidation of ketone bodies, helps to maintain capillary integrity and tends to interrupt the vicious cycle that is always set up between tissue edema and tissue anoxemia.

10. Bartlett, W., Jr.: Surg., Gynec. & Obst. **71**:450, 1940.
11. Coller, F. A., and Maddock, W. G.: Tr. Am. A. Study Goiter, 1933, p. 188.
12. Bartels, E. C.: New England J. Med. **218**:289, 1938.
13. Brown, R. B., and McCray, P. M.: Endocrinology **22**:302, 1938.

I have the support of Elliot [14] in the view that the acidosis of hyperthyroidism damages the capillaries, increasing their permeability, and that this may be responsible to a large extent for the decrease of plasma protein, particularly of the albumin fraction, by permitting the passage of protein from the capillaries to the tissues, where it tends to hold water. That this acidosis may decrease also the production of serum albumin by the liver through damage to the hepatic capillaries is more truly a matter of speculation but seems as reasonable as any other hypothesis in the light of present knowledge. Certainly, the diet of the patient with thyrotoxicosis who is being prepared for operation should be high in caloric intake with relatively large amounts of carbohydrate, a liberal allowance of protein and a small fat content. This is a decided reversal of the earlier practice of trying to attain a large caloric intake by diets with high fat intake and the limitation of protein for fear the specific dynamic action of the latter would increase basal metabolism.

SUMMARY

The essential biochemical derangement of thyrotoxicosis is an acidosis which is probably attributable in part to ketosis. The carbon dioxide–combining power of the plasma is maintained within normal limits even in severe exacerbations so long as the patient is at rest and his physiologic needs for water and nourishment are met, but a prompt decrease in alkali reserve occurs on exertion. During improvement on treatment preliminary to thyroidectomy and subsequent to operation, a profound fall in the total titratable acid of the urine, of the organic acids and of ammonia occurs, and the p_H of the urine rises if the patient's intake of food is kept constant quantitatively and qualitatively. In nearly 50 per cent of the patients who show prompt improvement after thyroidectomy, a rise in the alkali reserve of the plasma occurs.

I believe that acidosis bears a fundamental relation, probably causative, to the tendency of the patient with hyperthyroidism to water retention by the tissues through impairment of capillary integrity. The relation of this process to the loss of plasma protein from the blood to the tissues to the possible interference with serum albumin production by the liver and to the establishment of a vicious cycle of tissue edema and cyanosis is discussed. Appropriate therapy is mentioned.

University Club Building.

14. Elliot, J.: Personal communication to the author.

CYSTADENOMA OF THE PANCREAS

REPORT OF FIVE CASES

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Five patients with cystadenoma of the pancreas have been treated in the surgical department of the New York Hospital during the past nine years, and it is with the purpose of bringing out certain diagnostic features and operative findings that the 5 cases are hereinafter reported and discussed.

No attempt has been made to review the literature on pancreatic cysts, for this was done recently by Kennard [1] in 1941. However, certain publications are of special interest in regard to the incidence and the classification of these tumors. White [2] found 3 cases of pancreatic cyst, 1 of which was hydatid, in 6,708 autopsies at Guy's Hospital in London, England; Young,[3] 5 patients with cysts between 1920 and 1937 at the Massachusetts General Hospital, Boston; and Judd,[4] 88 who came to operation among a total of 723,397 patients admitted to the Mayo Clinic, Rochester, Minn. In a series of 121 cases of pancreatic cyst, Oser [5] found an equal distribution between the sexes (60 male and 61 female); and Kennard [1] stated that the cysts commonly appear in middle life. Boyd [6] classified pancreatic cysts as retention cysts, congenital cysts, cystadenomas and pseudocysts.

From the Department of Surgery, New York Hospital and Cornell University Medical College.

1. Kennard, H. E.: Papillary Cystadenocarcinoma of the Pancreas, Surgery **9**:65-79, 1941.

2. White, W. H.: Diseases of the Pancreas, Guy's Hosp. Rep. **54**:17-49, 1897.

3. Young, E. L., Jr.: Pancreatic Cyst, New England J. Med. **216**:334-339, 1937.

4. Judd, E. S.; Matson, H., and Mahorner, H. R.: Pancreatic Cysts: Report of Forty-Seven Cases, Arch. Surg. **22**:838-849 (May) 1931.

5. Oser, L.: Diseases of the Liver, Pancreas, and Suprarenal Glands, in Nothnagel, H.: Encyclopedia of Practical Medicine, Philadelphia, W. B. Saunders Company, 1903, p. 197.

6. Boyd, W.: A Textbook of Pathology, Philadelphia, Lea & Febiger, 1932, p. 528.

The most recent of our cases (case 1) is presented in detail to emphasize certain features, while the other 4 cases are abstracted more briefly.

REPORT OF CASES

CASE 1.—M. J., a white American-born woman aged 37 years, was admitted to the New York Hospital on Aug. 2, 1941. Her chief complaint was severe pain in the left upper quadrant of the abdomen of four days' duration.

The past history was remarkable only in that the patient had toxemia of pregnancy in 1933; she was delivered of a healthy child.

Nine years before admission, the patient began to have attacks of pain in the epigastrium and the left upper quadrant of the abdomen associated with nausea and vomiting. The pain radiated to the left side and the back and was cramplike. Five years before admission, cholecystectomy for stones was done elsewhere. There was only partial relief of the pain, and she continued to have three or four attacks per year of gnawing, aching pain in the left upper quadrant of the abdomen. Four years before admission, a mass was noted in the upper part of the abdomen. One year later, she was admitted elsewhere with severe attacks of pain in the upper part of the abdomen, and operation was advised but refused. Mild diabetes was found at this time. During the year before admission, the diabetes increased in severity so that she lost 40 to 50 pounds (18.1 to 22.7 Kg.) and had polyuria and polydipsia. Her family physician prescribed 45 units of insulin a day and effected good control of the diabetes. Two months before admission, the patient had a severe attack of pain in the left upper quadrant of the abdomen; four days before entrance into the hospital, cramplike pain developed in the epigastrium and the left upper quadrant of the abdomen, aggravated by deep breathing and associated with nausea and vomiting. The symptoms increased in severity until the time of admission. There was no bowel movement or passage of flatus during this attack.

Physical Examination.—The patient was a moderately obese, acutely ill white woman of stated age in mild distress. The temperature was 37.6 C. (99.7 F.), and the blood pressure was 125 systolic and 85 diastolic. The skin and the mucous membranes showed moderate dehydration. The abdomen was slightly distended and tense with diffuse tenderness in the left upper quadrant, muscle spasm and rebound tenderness. A questionably cystic mass, extending from the left flank to the midline and from the costal margin to the umbilicus could be outlined only with difficulty because of tenderness. No bruit or fluid was present. There was an umbilical hernia with a defect of 2 by 2 cm. Pelvic and rectal examinations were negative.

Laboratory Findings.—The urine gave a 3 plus reaction for sugar and a 2 plus reaction for acetone. The blood findings were: hemoglobin content, 14 Gm.; red blood cell count, 4,900,000; white blood cell count, 13,000. The Kline test was negative; the blood urea nitrogen was 13 and the blood sugar 237 mg. per hundred cubic centimeters.

Roentgen Examination.—A flat plate of the abdomen showed a soft tissue mass in the left upper quadrant not associated with the kidney or the spleen. A chest plate was negative except for pleural thickening. A gastrointestinal series showed the stomach to be displaced cephalad and anteriorly, but no intrinsic lesion was demonstrable. An enema of barium sulfate revealed the splenic flexure and the transverse colon to be displaced caudad. Intravenous pyelograms revealed that

the left renal pelvis never visualized satisfactorily. What could be seen of the upper calices did not appear abnormal. The kidney was of usual length and width. These findings led us to believe that the condition arose from the retroperitoneal space, with the left kidney and the tail of the pancreas recognized as the most likely sites of origin. Because of the downward displacement of the splenic flexure and the transverse colon and the medial and upward displacement of the stomach, the body or the tail of the pancreas seemed to be the probable site. The fact that the tumor was of a cystic nature suggested that we were dealing with a cyst in the body or the tail of the pancreas.

Hospital Course.—The patient was kept in bed and the diabetes regulated while the studies just mentioned were carried out. The pain, nausea and vomiting subsided, and the mass in the upper part of the abdomen became more readily outlined as the tenderness subsided.

Operation.—On the seventh day after admission, with the patient under anesthesia induced with open drop ether, an upper left rectus incision was made, and a large mass was encountered. It appeared to be beneath the gastrocolic omentum, which was stretched to allow for the displacement of the stomach and the transverse colon, and the significant finding was the tremendous enlargement and obvious dilatation of the blood vessels. After separating the gastrocolic omentum, the mass could be readily seen. It was roughly round, had a poorly circumscribed outline, was cystic to palpation and was only slightly movable. A large vein, 1 cm. in diameter, coursed transversely and obliquely over the anterior surface of the cyst. An incision was made into the cyst and about 1 liter of thick, glairy, curdlike fluid was aspirated. This collapsed the mass sufficiently to allow better inspection of the surroundings. The large vein was thought to be the splenic and was clamped, divided and ligated when it became obvious, after an attempt to dissect it off the mass, that it had to be sacrificed in order to remove the tumor successfully. By sharp and blunt dissection and further freeing of the vessels, the third portion of the duodenum was separated from the mass. It now became apparent that the growth arose from the pancreas in a broad pedicle involving the outer third and the tail of the organ. It was necessary to remove a small amount of the pancreas with the cyst, and this was accomplished without injury to the large pancreatic duct. Transfixion sutures were placed in the cut areas of the pancreas. Careful inspection was made to determine whether any other major vessels had been injured, and it was possible to show that the middle colic artery, the splenic artery and the portal vein had been preserved. We were correct in our assumption that the large vein which had been ligated was the splenic vein. As the spleen was enlarged to three times its normal size, splenectomy was performed. Four cigaret drains were inserted, and the abdomen was closed with through and through sutures of silver wire. The patient was in moderate shock during the latter third of the operation and on the operating table received a transfusion of 1,000 cc. of blood.

Postoperative Course.—Since the patient was in moderate shock, she was given oxygen by mask and 500 cc. of blood. The next day her condition was good. The diabetes, which was easily controlled for the first forty-eight hours, became difficult to manage for the next forty-eight hours. From the fifth day on, the patient's condition progressively improved so that 10 units of protamine zinc insulin sufficed to control the diabetes at the time of discharge instead of the 35 units of unmodified insulin and 10 units of protamine zinc insulin which previously had been required.

The serum amylase was 13 units per cubic centimeter on the third postoperative day; two weeks later, it was 100 units, and five days before discharge, it was 40 units.

The wound drained moderate amounts of serosanguineous fluid. Two drains were removed on the tenth, and the remaining two, on the eighteenth postoperative day. The silver wire sutures were removed on the twentieth postoperative day. At the time of discharge, the wound was healed except for a sinus tract, 4 cm. in depth and 0.6 cm. in diameter. There was never any excoriation of the skin.

Pathologic Findings.—Gross: The cyst measured 15 by 10 by 10 cm. The lining was smooth but with heavy pillow-like masses which contained fluid and represented daughter cysts. The outside of the cyst was smooth and well encapsulated. The spleen weighed 419 Gm. and measured 19 by 10 by 4.5 cm. The parenchyma was dark red with prominent follicles.

Microscopic: The cysts were lined with columnar epithelium thrown into irregular folds. The cells were regular, well differentiated and high columnar. The spleen showed questionable miliary tubercles.

Follow-up Examination.—Six weeks after discharge her condition was excellent. The diabetes was controlled by 10 units of protamine zinc insulin a day. The sinus tract had practically healed.

Case 2.—A. M., a white Danish-born woman 44 years of age, was admitted to the New York Hospital on Sept. 29, 1932, with a history of fatigue associated with vague abdominal distress and constipation of two years' duration. The past history was negative except that she had had adequate treatment for syphilis during the past three years.

The physical examination was essentially negative except for the abdomen, in which a well defined mass was felt in the left upper quadrant, extending from the costal margin to the midline. The mass was nontender and freely movable and descended slightly with inspiration.

The laboratory examinations were essentially negative except for the blood sugar, which ranged from 241 to 111 mg. per hundred cubic centimeters with decreased dextrose tolerance. A roentgen gastrointestinal series showed the stomach displaced to the left and downward by a mass superior to the lesser curvature. An enema of barium sulfate revealed the transverse colon to be displaced caudad.

Operation.—At operation through a left paramedian incision, a large (12 by 8 by 5 cm.) cyst arising from the midportion of the pancreas was removed through the gastrohepatic omentum. The wound was closed without drainage.

Pathologic Findings.—Gross: The specimen consisted of a cystic mass, 12 by 8 by 5 cm., with a small amount of pancreatic tissue attached to the posterior surface. The cyst was multilocular and was composed of two parts—a larger coalesced mass of cysts which was thin walled and blue and contained yellowish fluid and a rounded mass of small thin-walled cysts from a few millimeters to 3 cm. in diameter. It was transparent and white and contained a colorless fluid.

Microscopic: Microscopic examination showed a multilocular cyst lined with low cuboid epithelium thrown into papillary projections.

Postoperative Course.—During the postoperative course there was transient slight glycosuria and moderate acidosis. The wound healed by first intention.

Follow-up Examination.—Follow-up examination revealed that the patient had slight discomfort in the left upper quadrant of the abdomen for the first few months after operation. She had been in excellent health for the past eight years at the time of her last visit in July 1941.

CASE 3.—N. C., a white Russian-born Jewish woman 42 years of age, was admitted to the New York Hospital on May 18, 1934, with a history of attacks of epigastric pain radiating to the back and occurring approximately every month and lasting one to two days over the preceding four and a half years. During the seven months before admission, she had dull epigastric pain associated with frequent loose, foul stools. The latter cleared up after a few months. For several weeks before admission, the patient had noted a mass in the epigastrium.

The physical examination revealed an emaciated, chronically ill woman. The thorax was rachitic in contour. In the abdomen there was a visible epigastric mass which, on palpation, was nodular, measured 10 by 6 cm., was firm, nontender and immovable and transmitted the aortic pulsation.

The laboratory examinations were essentially negative except for the finding of decreased dextrose tolerance. A roentgen chest plate revealed soft mottling of the apexes, representing questionable tuberculosis. A gastrointestinal series showed the stomach to be displaced to the left by a mass, and a roentgenogram taken twenty-four hours after the gastrointestinal series showed the transverse colon to be depressed caudad.

Operation.—At operation, through a left rectus incision, a lobulated mass, 18 by 12 by 15 cm., was found lying in the region of the pancreas. The gallbladder was normal except for adhesions around it. A large (1 to 1.5 cm.) vein traversing the cyst was torn. By the time the hemorrhage was controlled, the patient had lost so much blood that she was in shock, and the procedure had to be abandoned. The abdomen was closed without drainage.

Postoperative Course.—During the postoperative course the patient failed to respond to multiple transfusions. Oliguria, renal and cardiac failure developed, and she died forty-eight hours after the operation. Permission for postmortem examination was refused.

CASE 4.—A. C., a white Irish-born woman 66 years of age, was admitted to the New York Hospital on Sept. 6, 1938, with a history of pain in the right upper quadrant of the abdomen associated with nausea and eructation and aggravated by the ingestion of fatty and greasy foods. All symptoms were worse during the seven months before admission. The gallbladder showed a fairly good roentgen shadow. For twenty years, she was known to have duodenal ulcer; this was interpreted as healed on roentgen examination shortly before admission. One and a half years before admission, a carcinoma of the cervix was treated with radium. There were no further clinical manifestations relative to this lesion.

The physical examination showed a thin well preserved woman. The heart sounds were of poor quality. The abdomen was soft with moderate tenderness in the right upper quadrant, and the edge of the liver was felt 3 cm. below the right costal margin. No mass was felt. Pelvic examination showed a firm band of scar tissue in the vagina, but the cervix was not seen or felt.

The preoperative laboratory examinations were essentially negative. A roentgenogram of the chest was negative, and a cholecystogram showed a normal gallbladder. A gastrointestinal series revealed a defect in the duodenal cap, but no soft tissue mass was seen. An enema of barium sulfate was not given.

Operation.—At operation the abdomen was opened through a right rectus incision. The liver showed a slight degree of cirrhosis, and the gallbladder was large. A tumor, 8 by 7 by 5 cm., lay beneath the stomach. This was attached to the body of the pancreas and was removed through a rent in the gastrocolic omentum. A large vein (the splenic) was incorporated in the wall of the cyst posteriorly. The

cyst was removed without injuring the vein. The gallbladder was removed, and one drain was inserted down to the foramen of Winslow.

Pathologic Findings.—Gross: The specimen was a thin-walled, lobulated cyst containing saliva-like fluid with milky sediment. Several calculi, approximately 1 mm. in diameter, were present in the wall.

Microscopic: The cyst was lined by high cuboid epithelium.

Postoperative Course.—During the postoperative course, the patient developed high blood and urine amylase with evidence of fat necrosis in the drainage. On the eleventh postoperative day there was noted in the left upper quadrant of the abdomen an abscess which necessitated drainage five days later. It was thought that the abscess was due to pancreatic damage and fat necrosis. The course was satisfactory after drainage, and the sinus tract healed completely two weeks after discharge from the hospital.

Follow-up Data.—The patient was known to be in excellent health at the time of her last report by letter, two years after operation.

CASE 5.—J. J., a white Gibraltar-born woman 54 years of age, was admitted to the New York Hospital on Jan. 4, 1939, with a history of a mass in the left upper quadrant of the abdomen of four years' duration, increasing in size slowly for three and one-half years and rapidly for the five months prior to admission. The patient had a dragging sensation in the back and had lost 20 pounds (9.1 Kg.). She had a "binding feeling" on defecation. The only relevant finding in the past history was that she had had an appendectomy fourteen years before admission.

The physical examination revealed a thin elderly appearing woman. The fundi showed arteriosclerotic changes of moderate degree. The abdomen was asymmetric, and there was a firm, slightly tender, movable mass, 19 by 15 cm., extending from the left costal margin to the midline and to the left flank. There was no bruit or expansile pulsation. There was a right rectus scar with a fascial defect, 8 by 5 cm. in diameter.

Laboratory examinations were entirely negative except for the stools, which gave a 2 plus reaction for benzidine. A chest plate roentgenogram was negative. A roentgen gastrointestinal series showed the stomach to be displaced medially and anteriorly. An enema of barium sulfate showed the transverse and decending parts of the colon displaced laterally and downward. Intravenous pyelograms were negative except for a soft tissue mass in the left upper quadrant of the abdomen below the spleen.

Operation.—At operation through a left rectus incision, a cystic mass arising from the tail of the pancreas was removed through a rent in the gastrocolic omentum. The abdomen was closed without drainage.

Pathologic Findings.—Gross: The cyst measured 18 by 12 by 13 cm. and weighed 1,805 Gm. It was multilocular with cysts averaging 3 cm. in diameter and filled with thick mucoid material, some of which appeared puriform.

Microscopic: The cyst was lined by high columnar epithelium which resembled gallbladder mucosa.

Postoperative Course.—The postoperative course was uneventful. The wound healed by first intention.

There was an attack of catarrhal jaundice with prompt recovery three months after operation.

Follow-up Examination.—She was in excellent health on July 1, 1941, two and one-half years after operation.

COMMENT

Certain significant findings which these cases have in common are shown in table 1, reference to which reveals that a definite history of antecedent biliary tract disease was present in 4 of the 5 cases. The rela-

TABLE 1.—*Diagnostic Features in Cystadenoma of the Pancreas*

Case	History of Biliary Tract Disease	Mass	Diabetes	Roentgen Examination of Diagnostic Value	Splenic Vein at Operation
1	Typical	Present	Moderate	Yes	Traversing cyst anteriorly
2	Suggestive	Present	Mild	Yes	No statement
3	Typical	Present	Mild	Yes	Traversing cyst anteriorly
4	Typical	No mass	None	No	Traversing cyst posteriorly
5	None	Present	None	Yes	No statement

TABLE 2.—*Data Obtained by Roentgen Examinations*

Case	Soft Tissue Mass	Gastrointestinal Series	After Enema of Barium Sulfate	Pyelogram
1	Seen in the left upper quadrant of the abdomen; not associated with the kidney or the spleen	Stomach displaced cephalad and anteriorly	Splenic flexure and transverse colon displaced caudad	Preoperative: left side never filled Postoperative: left side filled normally Right side normal throughout; (urologic opinion: pressure on blood supply)
2	Superior to the lesser curvature in the left upper quadrant of the abdomen	Stomach displaced to the left, downward, and elongated	Transverse colon depressed caudad	None
3	Superior to the lesser curvature in the left upper quadrant of the abdomen	Stomach displaced to the left and elongated	Transverse colon depressed caudad	None
4	None seen	Stomach not displaced	None	None
5	Seen in the left upper quadrant of the abdomen below the spleen	Stomach displaced medially and anteriorly	Transverse and descending colon depressed laterally and caudad	Normal

tion of disorders of the biliary tract to cystadenoma of the pancreas is of diagnostic interest, but from the viewpoint of pathogenesis its significance is open to question.

The only other finding of note in the history was the presence of an abdominal mass which had been observed for four years in 2 cases and

seven weeks in 1 case. No mass was noted by the patients in the other 2 cases.

All 5 of the patients were women whose ages ranged from 37 to 66 years.

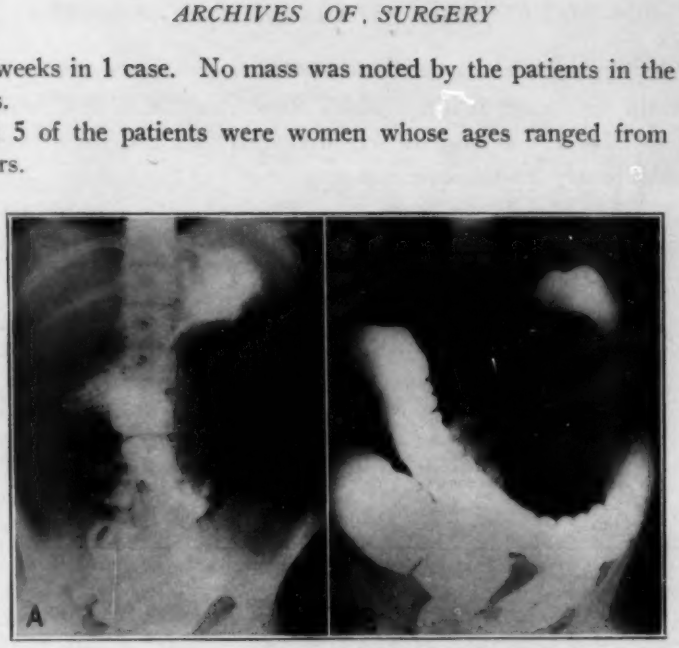

Fig. 1 (case 5).—Roentgenograms: *A*, from the gastrointestinal series showing displacement of the stomach medially by the pancreatic cyst; *B*, after an enema of barium sulfate showing displacement of the colon downward by the pancreatic cyst.

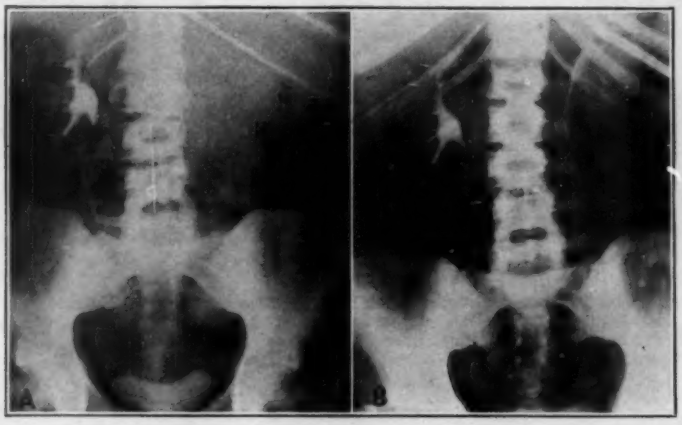

Fig. 2.—Intravenous pyelograms: *A*, preoperative, showing poor filling of the left renal pelvis (case 1); *B*, postoperative, showing normal filling of each renal pelvis (case 2).

The most important physical finding was the presence of a palpable, sometimes visible, mass in 4 of the 5 cases. The mass varied in size from 19 by 15 to 10 by 6 cm. In 2 of the 4 cases, the mass was movable; in

the other 2 it was fixed. In case 1, the mass was extremely tender on admission, but this was due to leakage of the cyst as was demonstrated at operation. The tenderness subsided during the preoperative course. Of the 3 remaining cases in which a mass was palpable, slight tenderness was present in only 1.

Fig. 3 (case 1).—High power photomicrograph showing tall columnar epithelium lining the folds of a cystadenoma.

Laboratory examination showed moderate diabetes in 1 case, mild diabetes in 2 cases and normal urine and blood sugar in 2 cases. In 2 cases there was increased severity of the diabetes shortly after operation. However, these manifestations were readily controlled. In 1 of the cases

(case 1), the diabetes was less severe at the time of discharge than it had been during the preoperative phase.

The most valuable laboratory test was the roentgen examination. As can be seen in table 1, roentgen examination was of diagnostic value in 4 of the 5 cases. In table 2, the results of the various roentgen examina-

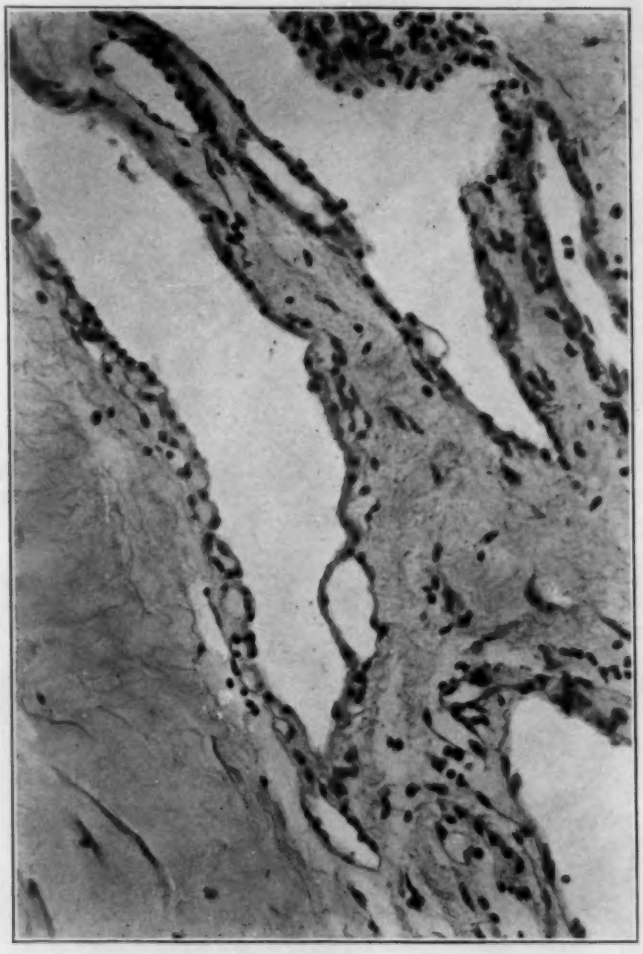

Fig. 4 (case 2).—High power photomicrograph showing low cuboid epithelium lining the cyst wall.

tions are shown. A soft tissue mass could be seen in the left upper quadrant of the abdomen in 4 of the 5 cases. In case 1, this shadow was distinguishable from those of the kidney and the spleen. Gastrointestinal series were made in all cases; in 4 there was definite displacement of the

stomach (fig. 1 *A*). The direction of the displacement varied from one case to another. Enemas of barium sulfate were given in 4 of the 5 cases; in all 4 the transverse colon was displaced caudad (fig. 1 *B*). Intravenous pyelograms were made of 2 patients; in 1, the shadows were normal, and in the other there was poor function of the left kidney and

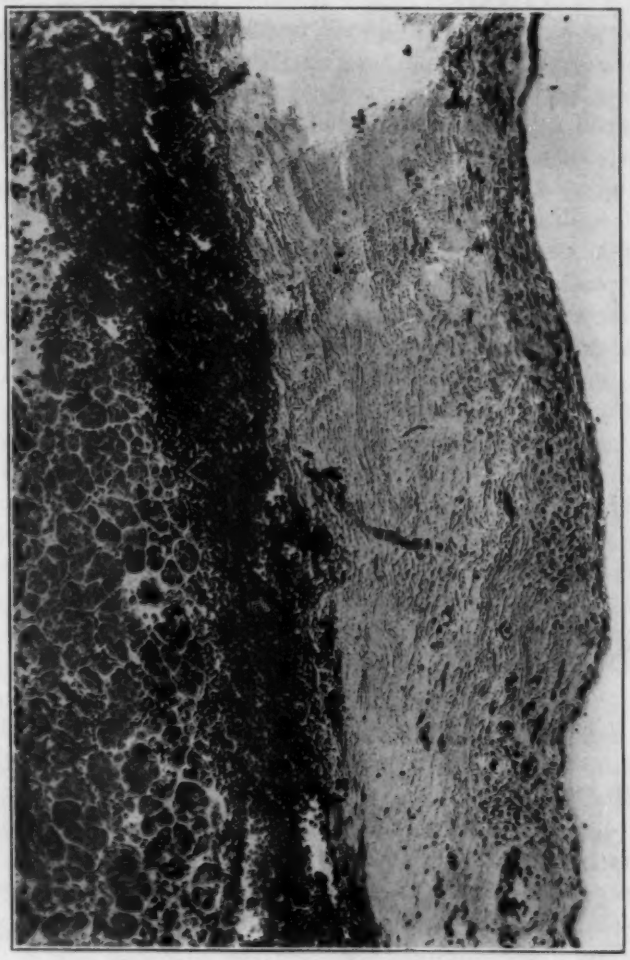

Fig. 5 (case 4).—Low power photomicrograph showing high cuboid epithelium lining the cyst. On the other side of the photomicrograph pancreatic acini are shown.

incomplete filling of the pelvis without change in its size or position. It was the clinical impression that pressure by the cyst on the renal artery or vein or both was the cause of this finding. This impression was proved subsequently by postoperative pyelograms which showed normal function of the left kidney and no filling defect (fig. 2).

An operative finding of great significance in this series of cases was the presence of a dilated splenic vein intimately associated with the wall of the cystadenoma of the pancreas in 3 of the 5 cases. Our attention was called to this finding most vividly by the most recent case in the group (case 1). In this instance, the splenic vein was adherent to the anterior wall of the cyst, crossing it transversely. During the course of the removal of the cyst, the splenic vein was injured and bled profusely until controlled by clamping. Following extirpation of the cyst, the spleen was found to be enormously enlarged; it was then removed. In retrospect, it is seen that removal of the cyst might have been facilitated by first removing the spleen. The great practical importance of this fact is seen in case 3, in which injury to this vein resulted in the death of the patient from hemorrhage and shock. In 1 other case, the vein was seen crossing the cyst anteriorly; in another it was found posterior to the cyst.

The gross and the microscopic pathologic appearance of these specimens were constant. The cysts were smooth, well encapsulated, multilocular and filled with clear or turbid fluid. Two of the cysts arose from the body and 2 from the tail of the pancreas far enough for the origin to be determined. The photomicrographs show the typical microscopic findings of true cystadenoma of the pancreas (figs. 3, 4 and 5). The cyst lining was of high columnar or cuboid epithelium with clear cytoplasm and basal nuclei. The lining was thrown into papillary projections. All 4 of the specimens showed this picture. Although no pathologic specimen was obtained in case 3, it is included in the series of cases because the clinical, roentgen and operative findings strongly suggested the diagnosis of cystadenoma.

SUMMARY

Five cases of cystadenoma of the pancreas are presented.

The significance of the history of antecedent disease of the biliary tract and of the presence of a mass in the upper part of the abdomen is emphasized.

Diabetes was present in 3 of the 5 cases, with improvement in the late postoperative period in 1.

Roentgen studies, such as gastrointestinal series, roentgenograms taken after enemas of barium sulfate and intravenous pyelograms, are of importance in establishing the diagnosis.

The intimate relation of the splenic vein to the wall of the cyst and the importance of its recognition during extirpation of the cyst are discussed.

FAMILIAL POLYPOSIS OF THE COLON

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URBANA, ILL.

By definition, polyposis of the colon is a condition in which adenomatous tumor grows from the wall of the bowel and projects into the lumen. Most authors adhere to the classification of Erdmann and Morris,[1] which divides polyposis into two types: (1) the adult or acquired type, which usually follows a chronic inflammatory process, such as chronic ulcerative colitis, tuberculosis or amebiasis; (2) the familial type, which involves the entire colon and rectum of young adults and shows a definite hereditary tendency. It is with this second type that this study is concerned.

The condition of polyposis was first described by Virchow [2] in 1863, and Cripps [3] presented 2 cases in 1882 in which he noted the hereditary factor. Since that time many studies have been published in the literature, and the heredofamilial malignant aspect of some cases has been emphasized. McKenney [4] studied three family groups, a total of 52 persons, and found 21 patients (40.39 per cent) with multiple polyposis; 8 of these (38.09 per cent) died of carcinoma of the rectum or the colon. In 1 of his patients malignant growth was found at the age of 15 years. The youngest patient was 2 years old, and 3 older children in the same family showed progressive increase in the size of the polyps. Lockhart-Mummery,[5] who also has presented studies of three families, expressed the belief that the condition is inherited as a mendelian dominant characteristic but that children are not born with it. Mayo and Wakefield,[6] Coffey and Bargen,[7] Hullsieck,[8] Rankin and Grimes,[9] Miller and Sweet [10] and Janssen [11] have all presented similar cases.

From the Department of Surgery, Carle Memorial Hospital.

1. Erdmann, J. F., and Morris, J. H.: Polyps of the Colon, Surg., Gynec. & Obst. **40**:460-468 (April) 1925.

2. Virchow, R.: Die krankhaften Geschwülste, Berlin, A. Hirschwald, 1863, p. 243.

3. Cripps, W. H.: Two Cases of Disseminated Polypus of the Rectum, Tr. Path. Soc. London **33**:165-168, 1882.

4. McKenney, D. C.: Multiple Polyposis of the Colon: Familial Factor and Malignant Tendency, J. A. M. A. **107**:1871-1876 (Dec. 5) 1936.

5. Lockhart-Mummery, J. P.: Causation and Treatment of Multiple Adenomatosis of the Colon, Ann. Surg. **99**:178-184 (Jan.) 1934.

6. Mayo, C. W., and Wakefield, E. G.: Disseminated Polyposis of the Colon: A New Surgical Treatment in Selected Cases, J. A. M. A. **107**:342-348 (Aug. 1) 1936.

(Footnotes continued on next page)

The purpose of this article is to study a family of 7 children in which 6 showed multiple polyps of the colon; 2 of these children died after carcinomatous degeneration.

FAMILIAL HISTORY

The paternal grandfather died at the age of 30 of cholera morbus. The significance of this can only be speculated on, but it is of interest in a family with a history such as this. The two doctors who attended him have long since died, and the only information available is that he died after an illness of fourteen hours' duration, having been previously in excellent health. The paternal grandmother died at the age of 32 of pulmonary tuberculosis. There were 4 sons in this family; 1 died at 30

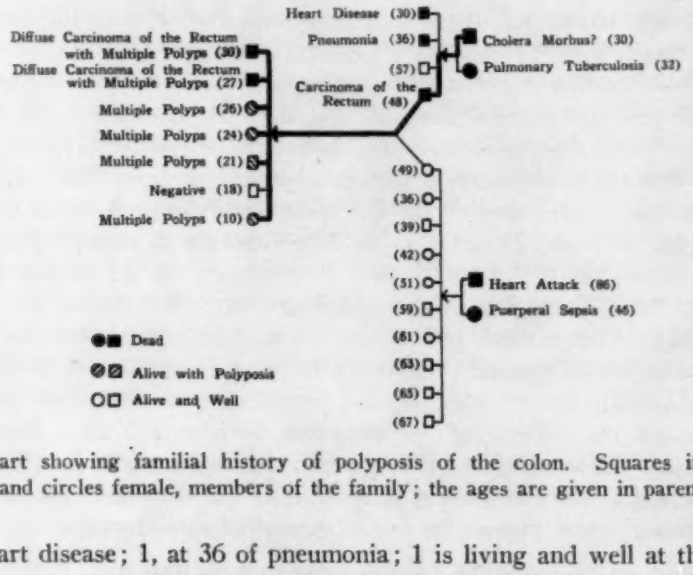

Chart showing familial history of polyposis of the colon. Squares indicate male, and circles female, members of the family; the ages are given in parentheses.

of heart disease; 1, at 36 of pneumonia; 1 is living and well at the age of 57 at the time of writing, and the fourth was the father of the 7 children in this study. The last named was seen elsewhere at the age of 47 with advanced carcinoma of the rectosigmoid. His wife relates that

7. Coffey, R. J., and Bargen, J. A.: Intestinal Polyps: Pathogenesis and Relation to Malignancy, Surg., Gynec. & Obst. **69**:136-145 (Aug.) 1939.

8. Hullsieck, H. E.: Multiple Polyposis of the Colon, Surg., Gynec. & Obst. **47**:346-356 (Sept.) 1928.

9. Rankin, F. W., and Grimes, A. E.: Diffuse Adenomatosis of the Colon, J. A. M. A. **108**:711-715 (Feb. 27) 1937.

10. Miller, R. H., and Sweet, R. H.: Multiple Polyposis of the Colon: Familial Disease, Ann. Surg. **105**:511-515 (April) 1937.

11. Janssen, C. L.: Familial Polyposis of the Colon with Carcinoma of the Rectum and Sigmoid, Ann. Surg. **95**:279-282 (Feb.) 1932.

he had had a twenty-four year history of diarrhea with blood and mucus in the stools and was known also to have "hemorrhoids" for many years. Although a diagnosis of multiple polyposis cannot be established, the history is typical of the condition. He died at the age of 48.

The maternal side presents an essentially negative history. The grandfather died at 86 after a heart attack and the grandmother at 46 of puerperal sepsis. There were 12 children on this side of the family; 2 died in infancy, and the rest are all living and well at the time of writing. The mother has always been well, and examinations of the colon and sigmoidoscopic examinations were negative.

REPORT OF CASES

CASE 1.—L. O'D., a 28 year old white man, was the first of the family to come to my attention. He was brought by ambulance to the Carle Memorial Hospital on Oct. 7, 1940, in a nearly comatose condition. The following history was obtained from the family: The patient, formerly a machinist, had been well until early in 1938 (two and one-half years previous to admission), when he complained of weakness and frequent loose stools accompanied by cramping pain. Blood had been noted in the stools several times. His local physician examined him and found "hemorrhoids and a small rectal tumor," which the physician fulgurated. He continued to have three or four loose stools a day, but the attacks of cramping pain were less frequent until about six months before admission, when he complained of bloating. Diarrhea and tenesmus then became worse. He had a roentgen examination of the colon which showed generalized polyposis. His physician advised surgical intervention and performed ileosigmoidostomy. The walls of the colon were found to be thick and uniformly studded with small round pea-sized polyps projecting from the mucosa into the lumen. Ileosigmoidostomy was followed by partial colectomy in two later stages. The patient fared badly after this series of operations, and when first seen at the Carle Memorial Hospital, he appeared markedly emaciated, cyanotic and dehydrated, and vascular collapse seemed imminent. There were multiple small bowel fistulas draining through the wall of the abdomen, and he had many loose stools daily in addition to copious drainage from the fistulas. Proctoscopic examination revealed a firm, somewhat fixed stenosing lesion in the rectum. Biopsy of this mass showed grade 2 adenocarcinoma. Peritonitis developed, and the patient died.

CASE 2.—L. L. O'D., a 30 year old brother of the patient in case 1, came to the clinic for examination on March 16, 1941 at my request. He had been well until 1938, when he had a brief episode of nausea, vomiting and diarrhea with cramping and bloody stools. In July 1939, he again had fever, nausea, vomiting and severe pain in the lower part of the abdomen. His physician noted marked abdominal distention and rigidity. Abdominal exploration was done to determine the cause of the peritonitis. A right rectus incision was made, and perforating carcinoma of the descending colon was found. Then through a left rectus incision the first stage of the Mikulicz operation was performed. On the following day, the tumor was removed by electrocautery. Later, cecostomy was done, and anastomosis was established between the proximal portions of the transverse colon and the rectum. Finally, the distal portion of the transverse colon and the descending colon were removed. After this, the patient got along well and returned to work. Later roentgen studies showed polyps in the remaining parts of the colon and

the rectum. The rectal polyps were cauterized and the "internal hemorrhoids injected." By the middle of 1940 he was complaining of pain low in the back and severe constipation. At the time of examination at the clinic, he was having seven or eight loose stools a day and was experiencing difficulty in starting the urinary stream. The wall of the abdomen showed multiple scars. On rectal examination there was a hard, baseball-sized mass in the prostatic region, blocking the rectum. Proctoscopic examination could not be attempted, but roentgen studies with barium sulfate contrast medium revealed extensive ulcerated carcinoma of the rectosigmoid. He was undergoing a series of roentgen treatments elsewhere at that time, but he has since died.

CASE 3.—M. O'D. H., a 26 year old sister of the patients in the first 2 cases, also came to the clinic for study at my request. Shortly after parturition in 1936, she began to have one to three watery stools a day. There was never any blood, but frequently mucus was noted. Three years later, she complained of generalized weakness and easy fatigability. Study of the colon in 1940 revealed generalized polyposis. Her physician did a first stage ileosigmoidostomy in August 1940, and she convalesced rapidly. At the time of writing she is having three to five soft stools a day. Her weight now is 99 pounds (45 Kg.). An enema of barium sulfate was given, and the ileocolostomy was found to be functioning well with innumerable polyps scattered throughout the colon. She stated that she "will never be operated on again." She was married and had one child.

CASE 4.—E. O'D. H., a 24 year old sister of the patients in the other 3 cases, came to the hospital on Jan. 21, 1941. She had no children. Because of diarrhea, the colon had been studied elsewhere, and a diagnosis of diffuse polyposis of the colon had been made. Proctoscopic examination here showed multiple polyps as large as 1.5 cm. in diameter. She was advised to undergo total colectomy, and on March 11 permanent ileostomy was established through a McBurney incision. Recovery was uneventful, and at the time of writing, the patient feels much better. It is expected that she will submit to the remaining stages of operation (total colectomy and posterior resection) in the near future.

CASE 5.—D. O'D., a 21 year old mechanic, was a brother of the previous 4 patients. He had no children. He submitted to examination at my request. He had always been well and presented no complaints. His history was generally noncontributory, and there were no bowel symptoms. Physical examination was likewise negative save for the rectum, in which many polyps were palpable, beginning about an inch (2.5 cm.) above the dentate margin. Sigmoidoscopy showed many polyps. The largest were about 8 mm. in diameter; many were pedunculated, and some occurred in clusters. Roentgen examination of the colon showed multiple polyps scattered through the large bowel except in the cecum and the ascending portion of the colon. At the time of writing, he is undecided about submitting to operation.

CASE 6.—V. O'D., a 10 year old schoolgirl and a sister of the other 5 patients, came to the clinic on March 16, 1941 for examination with the remainder of the family. The colon had been studied elsewhere and was believed to be normal. Two years previously, she had had an episode of cramping in the lower part of the abdomen associated with diarrhea, which persisted for about six weeks. She has no complaints at the time of writing and is gaining weight steadily. The colon was restudied here, and the roentgenologist stated that there were questionable minute polyps in the descending and the sigmoid colon. However, on sigmoidoscopy many tiny polyps were visualized which were about 3 mm. in

diameter. The family has been advised to have the roentgen and sigmoidoscopic examinations repeated annually and to consider operation after the child has passed adolescence.

CASE 7.—L. E. O'D. was 18 years old and a brother of the other 6 patients. His entire history and physical examination were negative. Roentgen examination of the colon and sigmoidoscopy were negative. Of the 7 children, this boy appeared to be the sturdiest. He was married and had one child.

DIAGNOSIS

The symptoms and signs commonly found include diarrhea, intermittent blood in the stools, abdominal cramping, loss of weight and anemia. Polyps may be palpable in the rectum, but sigmoidoscopy and roentgen examination of the colon establish the diagnosis definitely and reveal the extent of the disease.

TREATMENT

From a study of the literature it appears that carcinomatous degeneration of the polypi occurs frequently in cases of this disease. It is for this reason that total colectomy is considered the only satisfactory treatment. The most common procedure is that of establishing permanent ileostomy to divert the fecal stream, and after a satisfactory convalescence this is followed by total colectomy and finally by posterior resection of the rectum. Mayo and Wakefield [12] presented another method of treatment for use in selected cases. The rectum, the rectosigmoid and the sigmoid are first cleared of polyps by the repeated use of diathermy, only a few polyps being removed at a time. The second stage consists of end to side ileosigmoidostomy and hemicolectomy. As soon afterwards as possible, the third stage is carried out. This again consists of hemicolectomy with removal of the remaining transverse colon, the splenic flexure and the descending colon. Smith [13] observed a patient treated in this way for eight years; the patient returned frequently for fulguration of any new polyps but was able to return to heavy work.

McKenney [14] treated a number of patients with radiation therapy and reported that the number and the size of the polyps decreased but withheld recommendation of roentgen therapy until the results have been further evaluated.

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12. Mayo, C. W., and Wakefield, E. G.: Disseminated Polyposis of the Colon: A New Surgical Treatment in Selected Cases, J. A. M. A. **107**:342-348 (Aug. 1) 1936.

13. Smith, N. D.: Polypoid Disease of the Colon and Terminal Ileum: Observation of a Case for Eight Years, Proc. Staff Meet., Mayo Clin. **14**:255-256 (April 9) 1939.

14. McKenney, D. C.: Multiple Polyposis of the Colon: Familial Factor and Malignant Tendency, J. A. M. A. **107**:1871-1876 (Dec. 5) 1936.

SUMMARY

In a family of 7 children 6 were found to have polyposis—an incidence of 85.7 per cent. Among the 6 patients, there were 3 males and 3 females. In 2 (33 per cent), malignant change developed in the polyps. Both malignant changes were in males, but these were the oldest children.

The average age of the 6 is 19.7 years; the oldest was 30 and the youngest 10. None exhibited symptoms before the age of 23. The polyps in the younger children were proportionally smaller.

The father of these children died at the age of 48 of carcinoma of the rectum after a twenty-five year history suggestive of multiple polyposis. The paternal grandfather died at 30 of "cholera morbus"—an interesting fact.

Operation in 2 of these cases gave unsuccessful results. In both cases carcinomatous changes took place in the rectum. In a third case permanent ileostomy was done, and the patient will probably submit to total colectomy and posterior resection.

The 10 year old patient will be followed closely, and operation will be considered after she has matured.

Several of these patients have young children; these will present an interesting subject of study after a few years.

CONCLUSIONS

The type of polyposis presented in these cases is a hereditary condition.

Malignant degeneration of the polyps is frequent in cases of polyposis of the colon.

Early and radical operation is the treatment of choice.

GANGLION CELL TUMOR (GANGLIOGLIOMA) IN THE THIRD VENTRICLE

OPERATIVE REMOVAL WITH CLINICAL RECOVERY

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AND
LEO J. ADELSTEIN, M.D.
LOS ANGELES

Ganglion cell tumors of the brain are not common. However, owing to increasing interest in the subject during the past ten years these growths are now known to be less rare than once was believed. In 1937, Wolf and Morton [1] reviewed 48 cases of intracranial ganglion cell neoplasm found in the literature and added 2 of their own. In 14 cases in their review, the tumor arose in or near the third ventricle; the first case of this kind was described by Robertson in 1915.

No successful removal of a ganglion cell tumor in the third ventricle has been reported. The patient of Alpers and Grant [2] failed to survive partial extirpation. Dandy,[3] in his monograph, reported no cases of this kind, although in 3 of the cases he reported there were solid growths of uncertain cellular type resembling pineal tissue. In the majority of cases in which tumor in the third ventricle has been successfully operated on, the growth has been a so-called colloid cyst.

LITERATURE

The subject of ganglion cell tumor of the central nervous system was reviewed at length by Courville [4] in 1930 with the presentation of

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From the neurosurgical service of Dr. Carl W. Rand, Los Angeles County Hospital and the Department of Surgery (Neurological), University of Southern California School of Medicine.

1. Wolf, A., and Morton, B. F.: Ganglion Cell Tumors of the Central Nervous System, Bull. Neurol. Inst. New York **6**:453, 1937.

2. Alpers, B. J., and Grant, F. C.: The Ganglioneuromas of the Central Nervous System, Arch. Neurol. & Psychiat. **26**:501 (Sept.) 1931.

3. Dandy, W. E.: Benign Tumors in the Third Ventricle of the Brain: Diagnosis and Treatment, Springfield, Ill., Charles C. Thomas, Publisher, 1933.

4. Courville, C. B.: Ganglioglioma, Tumor of the Central Nervous System: Review of the Literature and Report of Two Cases, Arch. Neurol. & Psychiat. **24**:439-491 (Sept.) 1930; Gangliogliomas: A Further Report with Special Reference to Those Occurring in the Temporal Lobe, ibid. **25**:309 (Feb.) 1931.

2 cases and a summary of the 18 cases reported up to that time. He recommended the name "ganglioglioma," as first suggested by Ewing, because it indicates the two essential constituents of this neoplasm, i. e., ganglion and glial cells. Alpers and Grant also reviewed the literature on the subject and presented a case in which such a tumor arose from the floor of the third ventricle; the patient failed to survive exploratory operation. They expressed preference for the term "ganglioneuroma," as proposed by Pick and Bielschowsky [5] in 1911, because of the inherent simplicity of such a classification.

Seven cases of intracranial ganglion cell tumor were presented by Kernohan, Learmonth and Doyle.[6] In 2 of these cases, the tumor originated in the floor of the third ventricle. These authors used the terms "neuroblastoma" and "gangliocytoma," depending on the maturity of the ganglion cells.

An excellent review with a detailed consideration of the histopathology and a presentation of 2 cases is that of Wolf and Morton.[1] They offered a classification based on predominant cell types and cited two major groups: (1) the comparatively pure ganglion cell tumors—ganglioneuroblastoma and gangliocytoma, depending on cell maturity—and (2) the mixed ganglion cell and glial tumor, which include ganglioglioblastoma and ganglioglioma.

The commonest site of origin of these tumors in the brain is the region which, for purposes of classification, has been designated as the floor of the third ventricle. The next most common location is apparently the temporal lobe. This type of tumor occurs most frequently in young persons; a few cases have been reported in which the patients were over 40 years of age, but the majority are younger than that, and in about 60 per cent of the reported cases the patients are under 30 years of age.

Judging from the clinical and the pathologic picture, the tumor can be considered relatively benign. The duration of symptoms varies greatly but is recorded as high as sixteen years, and a span of two or three years is not uncommon. In a few cases, however, symptoms were noted only a few weeks before death. Wolf and Morton found a definite correlation between the microscopic appearance of the specimen and the clinical course, the duration of symptoms averaging eleven months for the more malignant ganglioneuroblastoma and five and one-tenth years for the mature variety, the ganglioglioma. Of course, the location of the lesion

5. Pick, L., and Bielschowsky, M.: Ueber das System der Neurome und Beobachtung an einem Ganglioneurom des Gehirns nebst Untersuchung über die Genese der Nervenfasern in "Neurinomen," Ztschr. f. d. ges. Neurol. u. Psychiat. **6**:391, 1911.

6. Kernohan, J. W.; Learmonth, J. R., and Doyle, J. B.: Neuroblastomas and Gangliocytomas of the Central Nervous System, Brain **55**:287, 1932.

creates a variable in any such estimation. In our patient, although the tumor arose within the third ventricle, symptoms had been present for at least three years.

In most instances, the neoplasm has been found at operation or necropsy to be fairly sharply demarcated from the brain substance and to have little tendency toward invasion. However, at times the mass is irregular with no boundaries and a strong tendency to invade the adjacent portion of the brain, as in 4 of the 6 cases presented by Kernohan, Learmonth and Doyle.[6] The microscopic picture in general has not given the appearance of a rapid growth but rather has tended to classify the mature varieties as fairly benign.

PATHOLOGIC DESCRIPTION

The pathologic characteristics have been discussed in detail by Courville, Wolf and Morton, Kernohan and others. Grossly, the tumor is usually gray, although sometimes it is multicolored, with areas of yellow pigmentation and hemorrhage. As mentioned previously, the mass is frequently, but not always, encapsulated; cyst formation is common, as are central necrosis and softening.

On microscopic examination, the striking feature is the presence of ganglion cells. These vary in size, shape and maturity, have one or more pale-staining nuclei and usually contain Nissl substance. Lymphocyte-like cells are usually found; the precise identity of these is not clear. They tend to be perivascular or diffuse and have been called "neuroblasts," [6] "medulloblasts" [7] and "lymphocytes." [1] In our case such cells were numerous throughout the tumor and particularly tended to form vascular cuffs in the manner of ordinary lymphocytic infiltration. Glial elements, present in varying quantity, aid in establishing a classification, as mentioned before. These cells vary from spongioblasts to large and well formed astrocytes and may be numerous or few.

REPORT OF A CASE

Gradual impairment of vision for three years with progressive development of headache, somnolence and vomiting. Ventriculography revealed bilateral symmetric internal hydrocephalus with complete absence of air in the third ventricle. Exploration of the third ventricle revealed a large tumor—ganglioma—which was completely removed. The patient made a good recovery.

C. R., a white boy 9 years of age, was admitted to the Los Angeles County Hospital on Oct. 30, 1939. His mother stated that subnormal vision had first been detected when the child began school three years before. In spite of numerous pairs of glasses, the failure of vision progressed to the point that the boy was taught braille and attended a school for the blind. Frontal headache,

7. Foerster, O., and Bagel, O.: Ein Fall von Ganglioglioma des Bodens des dritten Ventrikels, Ztschr. f. d. ges. Neurol. u. Psychiat. **145**:29, 1933.

although never a severe symptom, first appeared about two years before admission to the hospital and increased gradually but did not become incapacitating. In the last three months before admission to the hospital, the child manifested a marked tendency to somnolence, sleeping as many as twenty hours in the course of a day. Vomiting was frequent in the last two months; it tended to come on abruptly, often without nausea, and undoubtedly contributed to the loss of 15 pounds (6.8 Kg.) during this interval.

At no time had there been impairment of mentality or any alteration in personality. When aroused, the boy was active and, aside from the visual difficulty, presented no trouble with his gait nor any tendency to stagger.

Examination.—Examination revealed a rather poorly nourished but intelligent child who was able to cooperate well in neurologic testing.

Bilateral suboccipital tenderness was present together with resistance and pain on flexion of the neck. The sense of smell was intact. Visual acuity was greatly reduced, the boy being able to count fingers with the left eye at 6 feet (182.9 cm.) and with the right eye at 1 foot (30.5 cm.). Choked disks, apparently of long standing, were demonstrated in the fundi, although constant searching nystagmus made examination difficult. Left homonymous hemianopsia was thought fairly definitely to be present, and Wernicke's homonymous pupillary inaction sign appeared to be present when the right retina was tested. The left pupil was slightly greater than the right, although both were dilated and sluggish in reaction. There was considerable restriction of upward gaze.

Motor and sensory functions were intact in the extremities, and no ataxia, dysmetria or other cerebellar signs were noted. The reflexes were found to be normal throughout with equivocal bilateral Babinski signs.

Stereoroentgenograms of the skull (fig. 1 *A*) revealed the pronounced convolutional markings indicative of increased intracranial pressure of long standing. There was also some generalized separation of the cranial sutures. The pituitary fossa was enlarged, with beginning pressure erosion of the dorsum sellae turcicae.

Diagnosis.—The preoperative diagnostic impression was that the patient had either a craniopharyngioma (tumor or cyst of Rathke's pouch) or a neoplasm near the third ventricle, although the possibility of a midline cerebellar lesion could not be ruled out definitely.

Operation.—On November 9, ventriculography was carried out and demonstrated marked internal hydrocephalus, symmetric in outline with complete absence of air in the third ventricle (figs. 1 *B* and *C*). Preparations were made at once for right frontal craniotomy. With the concealed hair line incisional approach advocated by Dandy, a moderate-sized bone flap was outlined in the right frontal area and turned down without undue difficulty. The optic chiasm was inspected first to rule out the possibility of craniopharyngioma. The chiasm was found to be normal, although of a markedly prefixed type. An incision was made then through the right frontal cortex down to the dilated ventricle, interior inspection of which revealed a nubbin of tumor resting in and occluding the foramen of Monro. The foramen was gently enlarged, and a reddish vascular-appearing tumor mass was seen completely filling the anterior portion of the third ventricle. With careful blunt dissection, this mass was peeled away from the adherent walls of the ventricle and removed in toto. The wound then was given a careful toilet, with particular reference to all oozing points. The lateral ventricle was then filled with physiologic solution of sodium chloride. The lips of the cortical incision were allowed to approximate, the bone flap was returned to its correct

position, and the wound was closed in layers without drainage. Basal anesthesia induced with avertin with amylene hydrate, supplemented with ether vapor administered by nasal catheter, was used throughout the operation.

Postoperative Course.—The convalescent period was smooth and uneventful until the tenth postoperative day, when the patient became stuporous and a fever of 103 F. developed. Repeated tapping of the ventricular system caused a rapid fall of the temperature to normal, and the boy roused and became rational within a period of one week. The wound healed cleanly, and the patient was discharged from the hospital on December 7.

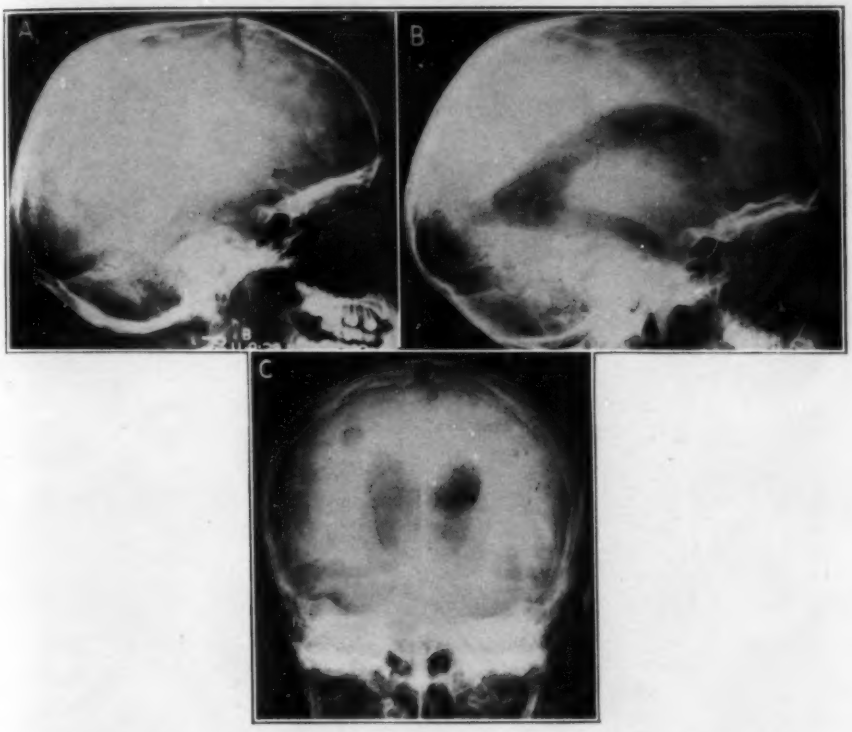

Fig. 1.—*A*, lateral roentgenogram of the skull indicating separation of sutures, increased convolutional markings and pressure erosion of the dorsum sellae turcicae. *B*, lateral ventriculogram showing marked dilatation of the ventricular system. *C*, anteroposterior ventriculogram showing symmetric internal hydrocephalus with complete absence of air in the third ventricle.

Unfortunately, this patient's vision was not improved by operation. During the year following operation, the boy was alert and active and grew about 4 inches (10.16 cm.) in height. For several months he was unable to sleep more than four or five hours per night, but this gradually lengthened to eight hours. He never showed any disturbance of water balance, but the temperature mechanism was considerably disturbed, the temperature during the day ranging from 96.4 to 97.6 F. He gained consistently in weight and strength (fig. 6).

Fig. 2.—Gross specimen of ganglioglioma from the third ventricle. Weight, 7 Gm.

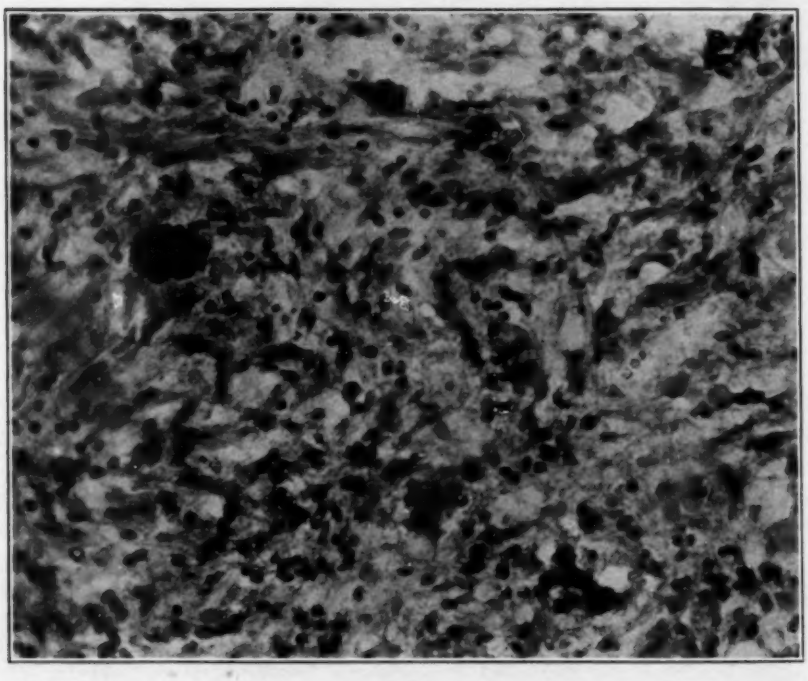

Fig. 3.—Photomicrograph of ganglioglioma showing the characteristic structure of the tumor, three ganglion cells, one with two nuclei (hematoxylin-eosin stain; × 276).

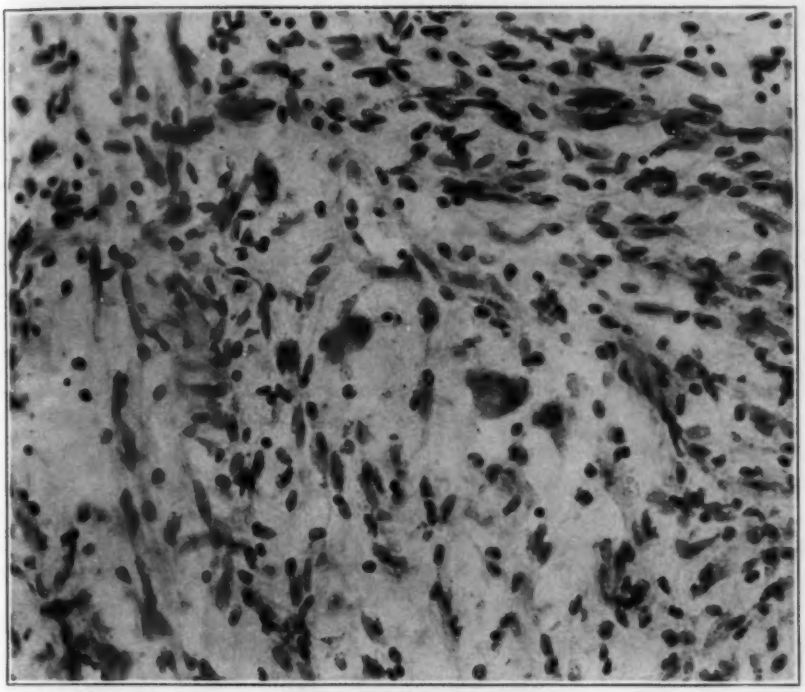

Fig. 4.—Photomicrograph of ganglioglioma (stained by cyanin method; × 276). Tigroid material can be fairly well made out in the center ganglion cell.

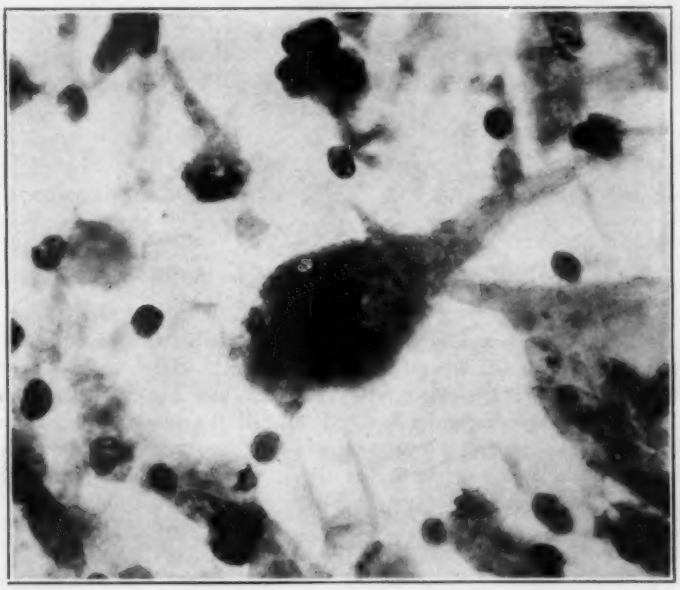

Fig. 5.—High power detail photomicrograph of nerve cells of ganglioglioma (hematoxylin-eosin stain; × 800).

Pathologic Examination.—The tumor measured approximately 3 by 4 cm. and weighed 7 Gm. (fig. 2). It was grayish pink, firm and irregularly nodular. There were a few discrete foci of hemorrhage evident on the surface, but the mass in general did not appear vascular. Histologic examination (figs. 3, 4 and 5) indicated a tumor mass made up of fibrous-like tissue in which the cells were in groups, strands or bundles. There was no definite regularity to their arrangement. A few foci of perivascular round cell infiltration were noted. Tumor giant cells were in evidence and, further, what were obviously nerve cells were found scattered throughout the growth. A section stained with the cyanin

Fig. 6.—Photograph of patient taken on April 18, 1941.

method showed a definite number of nerve cells of fairly adult type with typical vesicular nuclei; some of these had double nuclei. Many of the cells were bipolar and had nuclei elongated much like fibroblastic cells. Bielschowsky's method did not clearly demonstrate the details of the tumor, although isolated cells with threadlike processes evidently of nervous structure were seen occasionally. The stain also suggested that the great mass of the stroma forming the fibrous portion of the tumor was likewise of nervous origin. The diagnosis was ganglioglioma.

COMMENT

Surgical Aspects.—Tumors within the third ventricle present many well known obstacles to surgical treatment, and the operative results

have not always been encouraging. Before the report of Dandy [8] in 1921 of the successful extirpation of a colloid cyst, all third ventricle tumors had been discovered at autopsy rather than at operation. In 1933, 17 additional cases of primary neoplasm in this location were reported by Dandy,[8] with 2 deaths in the last 14 of the listed cases. In 1934, Masson [9] reported 2 cases in which removal was successful. Zimmerman and German,[10] Stookey,[11] Davidoff and Dyke [12] and Patterson and Leslie [13] also reported cases.

Postoperative deaths have been due to insurmountable damage to the essential elements in the region of the third ventricle, to postoperative intracranial hypertension and occasionally to late atresia of the cerebral aqueduct.

The majority of removable tumors are well encapsulated and, once removed, tend to recur slowly if at all. No recurrence of a colloid cyst has been reported, a fact which tends to bear out the suggestion of Sjövall,[14] reenforced by Zeitlin and Lichtenstein,[15] that these cysts are derived from remnants of the paraphysis. An estimate regarding recurrence of ganglion cell tumor in this location is, of course, not yet possible.

A frontal approach through the dilated lateral ventricle is, in the opinion of most authors, the technic of choice. Craniotomy in this location permits exploration of the chiasmal region first if suprasellar tumor is suspected; at the same operation the frontal lobe may be incised and the lateral ventricle entered. A core of frontal lobe may be excised to increase visibility if necessary. In this case the relation of the tumor and the surrounding structures was clearly outlined through the cortical incision without resort to partial frontal lobectomy. Neoplasms in the posterior portion of the third ventricle are of necessity attacked from

8. Dandy, W. E.: Diagnosis, Localization, and Removal of Tumors of the Third Ventricle, Bull. Johns Hopkins Hosp. **33**:188, 1922.

9. Masson, C. G.: Complete Removal of Two Tumors of the Third Ventricle with Recovery, Arch. Surg. **28**:527 (March) 1934.

10. Zimmerman, H. M., and German, W. J.: Colloid Tumors of the Third Ventricle, Arch. Neurol. & Psychiat. **30**:309 (Aug.) 1933.

11. Stookey, B.: Intermittent Obstruction of the Foramen of Monro by Neuro-Epithelial Cysts of the Third Ventricle, Bull. Neurol. Inst. New York **3**:446, 1934.

12. Davidoff, L. M., and Dyke, C. M.: Congenital Tumors in the Rostral Portion of the Third Ventricle, Bull. Neurol. Inst. New York **4**:221, 1935.

13. Patterson, J. E., and Leslie, M.: Colloid Cyst of the Third Ventricle of the Brain: Report of a Case Operated on with Recovery, Brit. M. J. **1**:920, 1935.

14. Sjövall, E.: Ueber eine Ependymcyste embryonalen Charakters (Paraphyse?) im dritten Hirnventrikel mit tödlichen Ausgang, Beitr. z. path. Anat. u. z. allg. Path. **47**:248, 1909.

15. Zeitlin, H., and Lichtenstein, B. W.: Cystic Tumor of the Third Ventricle Containing Colloid Material, Arch. Neurol. & Psychiat. **38**:268 (Aug.) 1937.

above through the corpus callosum. This approach is favored by Dandy unless the tumor is located at the anterior extremity of the ventricle.

Symptoms of Third Ventricle Tumors.—The various symptoms and signs which may be produced by tumors encroaching on the third ventricle have been the subject of considerable study. An excellent treatise on this subject was presented by Fulton and Bailey [16] in 1929. They cited the opinions of many workers before them (Weisenberg, Jumentie and Chausseblanche, Courtney and others) and reported 5 cases of their own, 4 with necropsy. The symptomatology was reviewed by Oldberg and Eisenhardt [17] in a series of 22 cases which they described in 1938 and by Nielsen and Raney [18] a year later. All of these writers noted a fairly constant symptom complex in the presence of third ventricle neoplasms.

The features described are: (1) hypersomnia, a frequent finding, felt to be due to encroachment on the posterior portion of the ventricle near the mouth of the cerebral aqueduct; (2) psychic disturbances, with loss of personality and memory, outbursts of anger, melancholy and mental dulness; (3) vegetative symptoms, including disturbances in temperature regulation, adiposity and genital dystrophy, circulatory dysfunction, such as blood pressure variations and "diencephalic epilepsy" (4) thalamic symptoms—painful hypesthesia, central pain; (5) pyramidal signs, such as facial weakness and Babinski signs; (6) "cerebel[illegible] signs, secondary to pressure on the frontocerebellar association tracts.

Acute headache, dizziness and fainting with change in position of the head have been recorded, but these are frequently not present and may be seen with tumors in other locations. Symptoms and signs, such as uncinate fits, visual field defects and disturbances of pupillary and extraocular motility, have been observed.

Our patient's somnolence was an outstanding complaint, but it is true that he had intracranial hypertension and hydrocephalus, making the evaluation of this symptom uncertain. He presented evidence of impairment in the right optic tract and considerable restriction of upward gaze, both of which were consistent with the diagnosis of a third ventricle neoplasm; but no other specific findings were present and at no time were there any aberrations of the mental status.

It is recognized that continued study and observation of cases presenting third ventricle tumors will lead to the diagnosis of a goodly percentage on the basis of symptoms and neurologic findings before

16. Fulton, J., and Bailey, P.: A Contribution to the Study of Third Ventricle Tumors: Their Diagnosis and Relation to Pathological Sleep, J. Nerv. & Ment. Dis. **69**:1, 145 and 261, 1929.

17. Oldberg, E., and Eisenhardt, L.: The Neurological Diagnosis of Tumors of the Third Ventricle, Tr. Am. Neurol. A. **64**:33, 1938.

18. Nielsen, J. M., and Raney, R. B.: Symptomatology of Tumors of the Third Ventricle, Bull. Los Angeles Neurol. Soc. **4**:1, 1939.

ventriculography is performed. At present, however, one hesitates to proceed with craniotomy in even the most classic case without the localizing benefit of ventriculographic study.

SUMMARY AND CONCLUSIONS

A case of a third ventricle tumor (ganglioglioma) with operative removal and clinical recovery is reported.

The most common site of origin of these ganglion cell tumors appears to be the floor of the third ventricle.

No definite clinical syndrome of a neoplasm in the third ventricle can be accurately described.

Ventriculography is indicated in every case in which the presence of the condition is suspected.

The chief operative procedures involving the removal of a third ventricle tumor are described.

INFLUENCE OF ABDOMINAL BINDERS ON LUNG VOLUME AND PULMONARY DYNAMICS

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AND
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Abdominal binders are used routinely after abdominal operations, and we have therefore studied the changes in pulmonary function caused by their application. The lung volume, its subdivisions and related aspects of pulmonary function have been measured before and after the application of abdominal swathes, and the possible relation of the findings to postoperative pulmonary complications has been considered.

MATERIAL AND METHODS

Studies were made on 8 subjects. Six subjects (1 to 6) were normal and ranged in age from 20 to 47 years; 3 (1, 5 and 6) were men. The other 2 subjects (7 and 8), respectively 53 and 59 years old, had pulmonary congestion due to chronic myocardial insufficiency; 1 (7) was a man. The method of Christie,[1] slightly modified,[2] was used, all measurements on normal subjects being made with the subject recumbent. In the patients with pulmonary congestion, the studies were made with the subject sitting at an angle of 80 degrees to the horizontal, since these persons could not tolerate abdominal binders when recumbent. Measurements were made both before and after the application of the binders, which extended from the symphysis pubis to just below the xiphoid process. The binders were applied with varying degrees of tightness to different subjects (table).

OBSERVATIONS

The volume of the functional residual air, composed of the reserve and residual airs, decreased in all the normal subjects after application of the binder, the decreases ranging from 1.1 and 6.3 per cent in those with snug binders to 15.0 and 20.4 per cent in those with tight binders; in the 2 patients with pulmonary congestion, moderately tight binders caused decreases in the functional residual air of 6.8 and 11.5 per cent,

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From the Medical Research Laboratories and Medical Service, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School.

1. Christie, R. V.: The Lung Volume and Its Subdivisions: I. Method of Measurement, J. Clin. Investigation **11**:1099, 1932.

2. Iglauer, A., and Altschule, M. D.: The Effect of Arterial and Venous Constriction Induced by Paredrine (p-Hydroxy-a-Methylphenylethylamine Hydrobromide) on the Lung Capacity and Its Subdivisions, Am. J. M. Sc. **201**:664, 1941.

as compared with 9.4 and 9.5 per cent in the normal subjects (table and chart).

The volume of the reserve air, one component of the functional residual air, decreased in all the normal subjects after application of the binder, the decreases ranging from 5.6 and 11.7 per cent in those with snug binders to 33.3 and 50.4 per cent in those with tight binders. In the 2 patients with pulmonary congestion, moderately tight binders

Data on the Influence of Abdominal Binders on Lung Volume and Pulmonary Dynamics in Eight Subjects

Subject	Functional Residual Air, Cc.	Reserve Air, Cc.	Residual Air, Cc.	Complemental Air, Cc.	Vital Capacity, Cc.	Total Capacity, Cc.	Tidal Air, Cc.	Respiratory Rate	Respiratory Minute Volume, Liters	Oxygen Consumption, Cc. per Minute	Comment
1	2,470	950	1,520	3,170	4,120	5,640	435	16	6.96	270	No binder
	2,315	835	1,480	3,210	4,045	5,525	385	21	8.10	259	Snug binder
2	1,685	715	970	2,500	3,215	3,985	515	7	3.61	188	No binder
	1,665	675	990	2,500	3,175	3,850	475	8	3.80	186	Snug binder
3	1,520	475	1,045	2,540	3,015	4,060	715	8	5.72	242	No binder
	1,375	355	1,020	2,500	2,855	3,875	535	11	5.89	233	Moderately tight binder
4	2,345	515	1,830	1,745	2,260	4,090	445	13	5.25	207	No binder
	2,125	395	1,730	1,625	2,020	3,750	525	14	7.35	217	Moderately tight binder
5	2,200	360	1,840	3,210	3,570	4,040	535	16	8.56	230	No binder
	1,870	240	1,630	2,660	2,900	3,530	475	18	8.55	240	Tight binder
6	1,835	555	1,280	3,410	3,965	5,245	475	15	7.13	286	No binder
	1,460	280	1,180	2,740	3,020	4,200	405	18	7.29	288	Tight binder
7*	3,310	710	2,600	2,060	2,770	5,370	595	16	9.90	293	No binder
	3,085	520	2,565	1,710	2,230	4,795	575	21	11.80	299	Moderately tight binder
8*	1,740	320	1,420	830	1,150	2,570	415	24	10.00	224	No binder
	1,540	80	1,460	790	870	2,330	435	26	11.30	213	Moderately tight binder

* Subject had pulmonary congestion due to chronic myocardiac insufficiency.

caused decreases in the reserve air of 26.8 and 75.0 per cent as compared with 23.3 and 25.3 per cent in the normal subjects (table and chart).

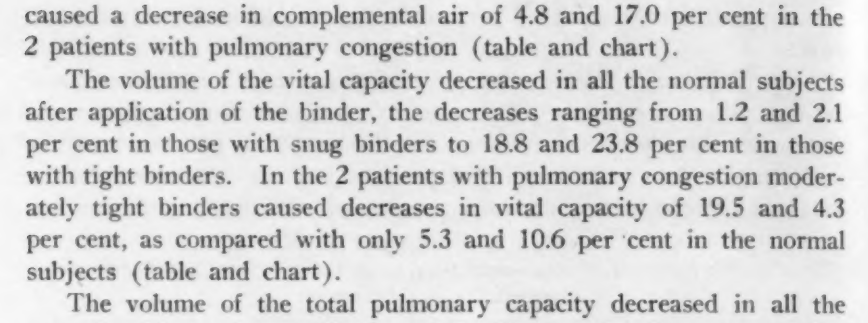
The volume of the residual air, the other component of the functional residual air, was unchanged after the application of snug or moderately tight binders to normal subjects and to those with pulmonary congestion. Tight binders caused slight decreases in residual air, i. e., 7.8 and 11.4 per cent, respectively, in the 2 subjects to whom they were applied (table and chart).

The volume of the complemental air was unchanged or slightly increased after the application of snug binders. Moderately tight and tight binders caused respective decreases in the normal subjects of 1.6 and 6.9 per cent and 17.1 and 19.6 per cent. Moderately tight binders

caused a decrease in complemental air of 4.8 and 17.0 per cent in the 2 patients with pulmonary congestion (table and chart).

The volume of the vital capacity decreased in all the normal subjects after application of the binder, the decreases ranging from 1.2 and 2.1 per cent in those with snug binders to 18.8 and 23.8 per cent in those with tight binders. In the 2 patients with pulmonary congestion moderately tight binders caused decreases in vital capacity of 19.5 and 4.3 per cent, as compared with only 5.3 and 10.6 per cent in the normal subjects (table and chart).

The volume of the total pulmonary capacity decreased in all the normal subjects after application of the binders, the decreases ranging from 2.0 and 3.4 per cent in those with snug binders to 12.6 and 19.9 per cent in those with tight binders. In the 2 patients with pulmonary



Changes in pulmonary function caused by the application of abdominal binders.

congestion moderately tight binders caused decreases in total capacity of 10.9 and 17.1 per cent, as compared with only 4.6 and 8.3 per cent in the normal subjects (table and chart).

The respiratory rate increased in all cases after application of the binder; the tidal volume decreased in 5 of the 6 normal subjects and 1 of the 2 patients with pulmonary congestion. The degree of tightness of the binder did not influence the amount of change in these measurements. The respiratory minute volume was unchanged in 4 of the 6 normal subjects, increasing in the other 2 and in both patients with pulmonary congestion. No changes in oxygen consumption occurred (table).

COMMENT

McMichael and McGibbon [3] showed that abdominal binders cause a cephalad shift in the position of the diaphragm. This results in

3. McMichael, J., and McGibbon, J. P.: Postural Changes in the Lung Volume, Clin. Sc. **4**:175, 1939.

decreases in functional residual and reserve airs, as the data of the present study show, varying with the degree of abdominal constriction. A tight abdominal binder, i. e., as tight as the usual postoperative binder, diminishes the functional residual air by 15 or 20 per cent. This implies a corresponding degree of pulmonary collapse and suggests that binders favor the occurrence of postoperative atelectasis. The decreases in functional residual air due to tight swathes also indicate that abdominal constriction causes a decrease in the negativity of the intrapleural pressure. In the present study it was found that tight abdominal binders cause decreases in functional residual air of 330 to 375 cc.; Christie and MacIntosh [4] found that the negativity of the intrapleural pressure decreased 2 to 3 cm. of water when the functional residual air diminished 200 to 350 cc. Decreased negativity of intrapleural pressure impedes peripheral venous return, as has been discussed elsewhere.[5] It has been shown also that abdominal binders may impede venous return from the legs by compressing the great veins of the abdomen.[6] These factors are clearly of importance as contributory causes in the genesis of postoperative shock and phlebitis.

The decrease in complemental air resulting from abdominal constriction also is of clinical significance. Many years ago Haldane, Meakins and Priestley [7] showed that prolonged maintenance of restriction of the tidal air, a portion of the complemental air, by means of abdominal or chest binders or other devices, results in fatigue of the respiratory center and anoxemia. This may be manifested by various respiratory arrhythmias, including Cheyne-Stokes respiration; the occurrence of such arrhythmias was noted in the present study.

It is clear that the application of tight abdominal binders, as practiced routinely after abdominal operations, favors atelectasis, has deleterious effects on respiratory function and impedes venous return. It is worthy of note that patients with pulmonary congestion show evidences, both by the measurements of this study and by clinical observation, of greatly increased dyspnea and a greater degree of respiratory embarrassment than normal subjects as a consequence of abdominal constriction.

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4. Christie, R. V., and MacIntosh, C. A.: The Measurement of the Intrapleural Pressure in Man and Its Significance, J. Clin. Investigation **13**:279, 1934.

5. Altschule, M. D., and Zamcheck, N.: Significance of Changes in the Subdivisions of the Lung Volume in the Trendelenburg Position, Surg., Gynec. & Obst., to be published.

6. Davis, D., and Gilman, S.: Factors Causing Increase in Venous Pressure of the Lower Extremities During Abdominal Operations, J. Clin. Investigation **20**:443, 1941.

7. Haldane, J. S.; Meakins, J. C., and Priestley, J. G.: The Effects of Shallow Breathing, J. Physiol. **52**:433, 1919.

SUMMARY AND CONCLUSIONS

The lung volume, its subdivisions and related aspects of pulmonary function have been studied in normal subjects and patients with pulmonary congestion before and after the application of abdominal swathes of varying degrees of tightness.

Decreases in functional residual air, varying with the degree of constriction, result from the application of abdominal binders. These changes indicate that atelectasis may occur as a consequence of abdominal constriction. Impairment of respiratory efficiency and venous return result from the decreased negativity of intrapleural pressure implied by diminution in the functional residual air.

Tight binders reduce the complemental air; this limitation of tidal expansion may give rise to fatigue of the respiratory center and anoxemia, resulting in respiratory arrhythmias.

SYMPATHECTOMY OF THE UPPER EXTREMITY

EVIDENCE THAT ONLY THE SECOND DORSAL GANGLION NEED BE REMOVED FOR COMPLETE SYMPATHECTOMY

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For a long time the standard sympathectomy of the upper extremity consisted of cervicodorsal ganglionectomy—removal of the inferior cervical and first and second dorsal ganglions.

In 1934, Freeman, Smithwick and White [1] began a series of studies which led to the employment of preganglionic sympathectomy in the treatment of Raynaud's disease of the upper extremity.[2] This was based on the proposition that the standard cervicodorsal ganglionectomy being postganglionic renders the vessels of the extremity more sensitive to circulating epinephrine. In 1936, Smithwick [3] proposed a preganglionic sympathectomy to be carried out as follows: The dorsal sympathetic chain is severed below the third dorsal ganglion. All rami to and from the second and third ganglions are severed, and the proximal end

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1. Freeman, N. E.; Smithwick, R. H., and White, J. C.: Adrenal Secretion in Man: The Reactions of the Blood Vessels of the Human Extremity, Sensitized by Sympathectomy, to Adrenaline and to Adrenal Secretion Resulting from Insulin Hypoglycemia, Am. J. Physiol. **107**:529, 1934. Smithwick, R. H.; Freeman, N. E., and White, J. C.: Effect of Epinephrine on the Sympathectomized Human Extremity: An Additional Cause of Failure of Operations for Raynaud's Disease, Arch. Surg. **29**:759 (Nov.) 1934.

2. J. F. Fulton (Physiology of the Nervous System, New York, Oxford University Press, 1938, p. 220) pointed out that W. K. Livingston (The Clinical Aspects of Visceral Neurology, Springfield, Ill., Charles C. Thomas, Publisher, 1935) was the first to do a modified form of preganglionic sympathectomy to the upper extremity. He was prompted, however, by the belief that removal of the inferior cervical and upper two dorsal ganglions does not constitute a complete sympathectomy to the upper extremity and apparently did not have epinephrine sensitivity of the sympathectomized vessel in mind.

3. Smithwick, R. H.: Modified Dorsal Sympathectomy for Vascular Spasm (Raynaud's Disease) of the Upper Extremity: A Preliminary Report, Ann. Surg. **104**:339-350, 1936; The Value of Sympathectomy in the Treatment of Vascular Disease, New England J. Med. **216**:141-150, 1937.

of the chain is sutured into the muscles of the back to insure against regeneration. To insure complete ramisectomy, segments of the second and third intercostal nerves are removed up to their emergence from the dura.

In 1935, Telford [4] proposed that preganglionic sympathectomy be done by severing the white rami of the second and third intercostal nerves and severing the sympathetic chain below the third dorsal ganglion.

In these operations all rami to and from the first intercostal nerve are left unmolested, and hence the completeness of sympathectomy is contingent on the absence of preganglionic fibers to the upper extremity in the first thoracic anterior root.

Kuntz [5] demonstrated as early as 1927 that the first thoracic nerve sends a white ramus into the stellate ganglion. He pointed out that since the first thoracic nerve contributes largely to both the median and the ulnar nerves, the sympathetic fibers contained in it (including those which enter via the ramus from the second thoracic nerve, whenever this ramus is present) are relatively widely distributed to blood vessels and other tissues in the upper extremity. In 1938, Kuntz, Alexander and Furcolo [6] demonstrated by histologic methods that the white ramus of the first thoracic nerve is important in supplying sympathetic nerves to the upper extremity. They stated:

> . . . If the distribution of preganglionic fibers of the first thoracic nerve in man corresponds to the distribution of these fibers in the cat and the dog, sympathetic denervation of the blood vessels in the upper extremity in man obviously cannot be accomplished by any operative procedure which leaves intact the first thoracic nerve with its communicating ramus and the inferior cervical ganglion with the gray communicating rami which connect it with the nerves which make up the brachial plexus.

Kuntz further showed that stimulation of the ventral root of the first, the second or the third thoracic nerve results in activation of sweat glands in the paw pads and constriction of cutaneous vessels of the foot. He concluded that:

> . . . Both the anatomic and the physiologic findings indicate that preganglionic components of the first thoracic nerve play an important role in the sympathetic innervation of the upper extremity both with regard to the sweat glands and the vascular musculature.

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4. Telford, E. D.: The Technique of Sympathectomy, Brit. J. Surg. **23**:448-450, 1935; Sympathetic Denervation of the Upper Extremity, Lancet **1**:70-72, 1938.

5. Kuntz, A.: Distribution of the Sympathetic Rami to the Brachial Plexus: Its Relation to Sympathectomy Affecting the Upper Extremity, Arch. Surg. **15**: 871-877 (Dec.) 1927.

6. Kuntz, A.; Alexander, W. F., and Furcolo, C. L.: Complete Sympathetic Denervation of the Upper Extremity, Ann. Surg. **107**:25-31, 1938.

The results of Kuntz's work were based on the findings in animals and do not agree with the findings in man.

Whether and to what extent the type of sympathectomy proposed by Smithwick and by Telford is a preganglionic sympathectomy and whether this type of sympathectomy solves the problem of Raynaud's disease of the upper extremity are matters that will be reserved for further publications. It is our purpose at present to show only that the first thoracic anterior root in man contains no sympathetic fibers to the upper extremity and that hence the operation as performed by Smithwick and by Telford is a complete sympathectomy so far as central connections are concerned. Furthermore, since Smithwick based his conclusions of completeness of sympathectomy on the psychogalvanic reflex,[7] we feel that it is of value to report our results based on another method —Minor's starch-iodine sweating test.[8]

Fig. 1 (case 1).—Patient after thermoregulatory sweating test. There was complete anhidrosis on the right down to the skin level of the third dorsal segment and including the right upper extremity. Only the second dorsal sympathetic ganglion was removed.

REPORT OF CASES

CASE 1.—N. B., a white woman 42 years of age, had gastric crises of tabes dorsalis.

7. Smithwick, R. H.: Surgical Intervention on the Sympathetic Nervous System for Peripheral Vascular Disease, Arch. Surg. **40**:286-306 (Feb.) 1940.

8. Minor, V.: Eines neues Verfahren zu der klinischen Untersuchung der Schweissabsonderung, Deutsche Ztschr. f. Nervenh. **40**:286-306, 1940.

Operation.—Bilateral anterior chordotomy at the second thoracic segment was done on July 6, 1940. With the patient's permission, the second dorsal sympathetic ganglion only was removed on the right. She was relieved of the pain of gastric crises.

Thermoregulatory Sweating Test.—This test was repeated several times with the same result. The photograph shown in figure 1 was taken on Sept. 16, 1940. The zone of anhidrosis on the right was complete and equivalent to that which results from the standard cervicodorsal ganglionectomy (removal of the inferior cervical and upper two dorsal ganglions).

Fig. 2 (case 2).—Patient after thermoregulatory sweating test. There was complete anhidrosis down to the skin level of the third dorsal segment on the left and the fourth dorsal segment on the right. On the left, the inferior cervical and upper two dorsal ganglions were removed. On the right, all rami to and from the second and third ganglions were severed, and the chain was sectioned below the third ganglion.

Case 2.—E. V., a white woman 45 years of age, had Raynaud's disease.

Operation.—On Aug. 19, 1940, on the right, the sympathetic chain was sectioned below the third dorsal ganglion. All rami to and from the second and third dorsal ganglions were severed, and the proximal end of the chain was sutured to the nearest muscle of the back. The rami to and from the inferior cervical and first dorsal ganglions were not molested. On the left, the inferior cervical and upper two dorsal ganglions were removed.

Thermoregulatory Sweating Test.—Anhidrosis was complete down to the third dorsal segment on the left and down to the fourth dorsal segment on the right (fig. 2).

CASE 3.—M. G., a white girl 22 years of age, suffered from migraine.

Operation.—On Oct. 2, 1940, on the right side, the sympathetic chain was sectioned below the third dorsal ganglion. Segments of the second and third

Fig. 3 (case 3).—Patient after thermoregulatory sweating test. There was complete anhidrosis down to the skin level of the third dorsal segment on the left and the fourth dorsal segment on the right. On the left, all rami to and from the second dorsal ganglion were severed, and the chain was sectioned below the second ganglion. On the right, segments of the second and third intercostal nerves were removed proximal to their rami, and the chain was sectioned below the third ganglion. *A*, front view; *B*, back view.

intercostal nerves were removed from the sympathetic chain almost to the spinal dura so that the sensory ganglions were included. All rami were left intact, and

the proximal cut end of the chain was sutured to the nearest muscle of the back. On the left side, all rami to the second dorsal ganglion were severed, a segment of the second intercostal nerve was removed, and the chain was sectioned below the second ganglion.

Thermoregulatory Sweating Test.—This test was repeated several times with the same result. The photograph shown in figure 3 was taken on March 13, 1941.

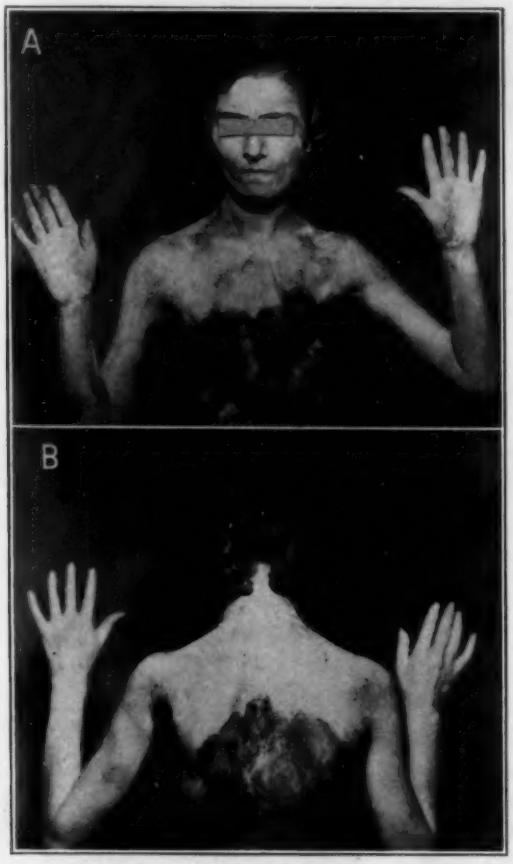

Fig. 4 (case 4).—Patient after thermoregulatory sweating test. There was complete anhidrosis down to the skin level of the third dorsal segment on the left and the fourth dorsal segment on the right. On the left, the second dorsal ganglion only was removed. On the right, all rami to and from the second and third ganglions were severed, and the chain was sectioned below the third ganglion. *A*, front view; *B*, back view.

Anhidrosis was complete down to the third dorsal segment on the left and down to the fourth dorsal segment on the right.

The influence of the sympathectomy on the migraine was disappointing.

CASE 4.—M. S., a white woman 26 years of age, had Raynaud's disease.

Operation.—On Jan. 4, 1941, on the right, all rami to and from the second and third dorsal ganglions were severed; the chain was sectioned below the third ganglion, and the cut end of the proximal chain was sutured to the nearest muscle of the back. On the left, the second dorsal ganglion only was removed.

Thermoregulatory Sweating Test.—Anhidrosis was complete down to the third dorsal segment on the left and down to the fourth dorsal segment on the right (fig. 4).

Fig. 5 (case 5).—Patient after thermoregulatory sweating test. There was complete anhidrosis down to the skin level of the third dorsal segment on the left. Only the second dorsal ganglion was removed on the left.

CASE 5.—R. R., a white man 38 years of age, had amputation stump pain on the left and pain in the fantom hand.

Operation.—The injection of procaine hydrochloride about the upper dorsal ganglions on the left markedly relieved the pain. On Nov. 19, 1941, the second dorsal ganglion only was removed on the left.

Thermoregulatory Sweating Test.—Anhidrosis was complete down to the third dorsal segment on the left (fig. 5).

COMMENT

Although this is not the place to discuss results other than those implied by the title, we would like to say that the relief of pain in case 5 has been complete to the time of writing (two months). This implies that relief of "sympathetic" pain in parts other than viscera is due to interruption of the efferent sympathetic supply as opposed to interruption of sympathetic afferents. We are dispelling the doubt we formerly entertained in this connection.

The amputation stump, which felt cool before operation, became 3 degrees warmer than a corresponding place on the right forearm. This increase in warmth was far greater than we had ever obtained on this part of the intact forearm after sympathectomy. Such a result has its implications in relation to the fact that only the terminal ends of the extremities become warmer after sympathectomy.[9]

Capillary Flushing Test.—We [9a] have previously shown that sympathectomy abolishes the capillary flushing that is caused by severe heating. The flushing is centrally controlled, and the fibers which subserve the capillary dilatation course through anterior roots and the thoracolumbar sympathetic chain. They parallel the course of sweat fibers.

In all of the patients described, the abolition of centrally controlled capillary dilatation coincided as nearly as we could tell with the anhidrosis. In cases 1 and 5, in which the sympathectomy was unilateral and only the second dorsal ganglion was removed, this fact was made obvious. The demarcation between the flushed and unflushed zones on the face was as marked after heating the body as it is after unilateral cervicodorsal ganglionectomy.

Epinephrine Test.—Repeated measurements of finger temperature in cases 2, 3 and 4 indicated no essential differences on the two sides. Skin temperatures were followed in the usual way while epinephrine was injected intravenously (1:250,000 at 40 to 60 drops per minute). The drop in temperature of the fingers was essentially the same on the two sides. The studies were made after time for degeneration had elapsed. The details of these studies are reserved for an appropriate publication, but they have a bearing on what we feel to be true—that removal of only the second dorsal ganglion results in the maximal effects and benefits that can be derived from sympathectomy of the upper extremity.

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9. Hyndman, O. R., and Wolkin, J.: (*a*) The Autonomic Mechanism of Heat Conservation and Dissipation: I. Effects of Heating the Body; Evidence for the Existence of Capillary Dilator Nerves in Anterior Roots, Am. Heart J. **22**:289-304, 1941; (*b*) Effects of Cooling the Body: A Comparison of Peripheral and Central Vasomotor Responses to Cold, ibid. **23**:43-58, 1942.

In all of the 5 cases reported, the rami to and from the inferior cervical and first dorsal ganglions were left intact. Hence all preganglionic fibers which course in the first thoracic anterior root were preserved. Nevertheless, thermoregulatory anhidrosis and abolition of centrally controlled capillary dilatation were as complete as they are when the inferior cervical and first dorsal ganglions are included in the sympathectomy. Hence it can be deduced that there are no preganglionic sympathetic fibers in the first thoracic anterior root, the connections of which are destined for the sweat glands or capillaries.[10] The statement could probably be made to include all skin structures and deeper vessels of the parts under consideration.

In the second case, a standard cervicodorsal ganglionectomy was done on the left, while on the right, the inferior cervical and first dorsal ganglions were left intact. After the operation, the left upper extremity was painful for several months. The burning pain appeared to be similar to that in peripheral neuritis and was so distressing that it offset the good results due to sympathectomy. In our experience, we have frequently encountered a pain of this type after cervicodorsal ganglionectomy, and we believe it to be a traumatic neuritis or neuralgia referable to the manipulation of the cords of the brachial plexus when the stellate ganglion is removed. We [11] called attention to this in a previous report and pointed out that Adson [12] had experience with the same complication. The patient's right upper extremity was comfortable and devoid of pain so that the result in that extremity was satisfactory to the patient and to us.

It may well be that the poor results from the treatment of Raynaud's disease of the upper extremity by cervicodorsal sympathectomy and the better results which have followed the Smithwick operation are referable to this complication which attends the former method rather than being referable to the difference between preganglionic and postganglionic sympathectomy. The complication naturally does not follow a lumbar ganglionectomy for the lower extremity. We have recently submitted

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10. The only possible arrangement that could make this statement untrue is one in which supposed preganglionic fibers in the first thoracic root coursed downward in the sympathetic chain to synapse with postganglionic neurons below the third dorsal ganglion and that the latter coursed up the chain again to emerge in the gray rami of the inferior cervical and first dorsal ganglions. Such an arrangement is hardly likely.

11. Hyndman, O. R., and Wolkin, J.: Raynaud's Disease: A Review of Its Mechanism; Evidence That It Is Primarily a Vascular Disease, Am. Heart J. **23**:535-554, 1942.

12. Brown, G. E., and Adson, A. W.: Physiologic Effects of Thoracic and of Lumbar Sympathetic Ganglionectomy or Section of the Trunk, Arch. Neurol. & Psychiat. **22**:322-357 (Aug.) 1929.

evidence [11] which supports Lewis' contention that Raynaud's disease is primarily a vascular abnormality and not primarily an abnormality of the sympathetic system. Hence while sympathectomy is beneficial, it does not effect a cure of the abnormality.

In any case, we feel that these and other studies lead definitely to the conclusion that it is not necessary to remove the stellate ganglion (inferior cervical and first dorsal ganglions) to effect a complete efferent sympathectomy to the face and the upper extremity. The additional procedure is superfluous and often fraught with a complicating pain that is probably a traumatic neuralgia. In dealing with sympathetic pain syndromes (amputation stump pain, causalgia and angina pectoris), we are developing the conviction that any relief of pain from sympathectomy, insofar as the extremities are concerned, is due to the interruption of efferent sympathetic pathways.

Our results have not convinced us that the more elaborate preganglionic sympathectomy [13] as proposed by Smithwick is more beneficial than removal of only the second dorsal ganglion, and hence we suggest that a removal of only the second ganglion should give optimal results with a minimal amount of operation and minimal complications.

The second anterior thoracic root contains many preganglionic fibers to the upper extremity, and hence for complete sympathectomy it is necessary that all connections from the second thoracic nerve be severed. We [14] reported 2 cases of extensive anterior rhizotomy in which the second thoracic roots were left intact. Thermoregulatory sweating on the upper extremities was abundant. In fact, in 1 case, sweating was abundant down to the skin level of the sixth dorsal segment. Recently, Atlas [15] reported a case in which the second dorsal ganglion was removed on the right side and the third dorsal ganglion on the left. The right hand became anhidrotic, while the left continued to sweat.

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13. And indeed to just what extent the Smithwick operation is a preganglionic sympathectomy remains to be proved. Both clinical (Hyndman and Wolkin [14]) and experimental studies (Geohegan, W. A., and others: The Spinal Origin of the Preganglionic Fibers to the Limbs in the Cat and Monkey, Am. J. Physiol. **135**: 324-329, 1942) have shown that preganglionic sweat fibers the connections of which are destined for the upper extremity course through anterior roots below as well as above the fifth dorsal segment and as far down as the eleventh dorsal segment. It is likely that many of their synapses with postganglionic neurons occur in ganglia below the third dorsal.

14. Hyndman, O. R., and Wolkin, J.: Sweat Mechanism in Man: Study of Distribution of Sweat Fibers from the Sympathetic Ganglia, Spinal Roots, Spinal Cord and Common Carotid Artery, Arch. Neurol. & Psychiat. **45**:446-467 (March) 1941.

15. Atlas, L. N.. The Role of the Second Thoracic Spinal Segment in the Preganglionic Sympathetic Innervation of the Human Hand: Surgical Implications, Ann. Surg. **114**:456-461, 1941.

CONCLUSIONS

Removal of only the second dorsal sympathetic ganglion results in as complete a sympathectomy insofar as central connections are concerned as does removal of the inferior cervical and upper two dorsal ganglions (the standard cervicodorsal ganglionectomy).

Hence no sympathetic fibers which supply the skin structures of the face and the upper extremity reside in the first anterior thoracic root in man. Operative removal of only the second dorsal ganglion is a simple procedure which insures a complete sympathectomy to the upper extremity and optimal physiologic results that can be attributed to efferent sympathectomy.

INTERMITTENT VOLVULUS OF THE MOBILE CECUM

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Partial volvulus of a mobile cecocolon is a definite but rarely suspected cause of intermittent pain in the right lower quadrant of the abdomen. Usually the diagnosis of this disorder is not established until an obvious attack of intestinal obstruction occurs and laparotomy demonstrates the cecal volvulus. It then becomes evident that the chronic symptoms which antedated the acute episode were occasioned by similar but partial and transitory torsion of the mobile cecocolon. The purpose of the present report is to demonstrate that by means of recently developed technics in the field of gastrointestinal investigation, the diagnosis of mobile cecum with intermittent volvulus can at times be established during the chronic preobstructive phase of the disease.

The term "mobile cecum" must be clearly defined, for in some respects it is discredited by the same stigma which now appertains to the words "visceroptosis" and "intestinal putrefaction." Strictly speaking, the mobile cecum is, according to Harvey,[1] no abnormality at all, and Berry [2] showed that the cecum in all but 6 per cent of persons is completely invested by peritoneum and carries no mesentery. Unmindful of this fact, surgeons in the first part of the twentieth century carried out numerous cecopexies in order to prevent kinking and twisting of the unattached cecum.[3] Their overenthusiasm caused the whole conception of the mobile cecum to fall into disrepute and obscured the fact that in some of the cases not only the cecum but also the ascending colon was endowed with mobility. Nonfixation of the ascending colon is a definite abnormality, which, if extensive enough, may predispose toward acute cecal volvulus or its chronic counterpart.

From the Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

1. Harvey, S. C.: Congenital Variations in the Peritoneal Relations of the Ascending Colon, Caecum, Appendix, and Terminal Ileum, Ann. Surg. **67**:641, 1918.

2. Berry, R. J.: The Caecal Folds and Fossae and the Topographical Anatomy of the Vermiform Appendix, Edinburgh, William F. Clay, 1897.

3. Wilms: Das Coecum mobile als Ursache mancher Fälle von sogenannter chronischer Appendicitis, Deutsche med. Wchnschr. **34**:1756, 1908. Waugh, G. E.: The Morbid Consequences of a Mobile Ascending Colon, with a Record of One Hundred and Eighty Operations, Brit. J. Surg. **7**:343, 1920. Houston, W. R.: The Mobile Right Colon, J. A. M. A. **93**:766 (Sept. 7) 1929.

A mobile right side of the colon represents an anomaly of fixation, a process which is considered to be the fourth and last stage in the embryologic development of the large bowel. After the first three stages —those of migration, rotation and descent—have taken place, the right side of the colon usually becomes fixed to the posterior parietal wall by obliteration of its mesentery. When some or all of this mesentery persists, a mobile cecocolon ensues, the degree of mobility being determined in part by the width and the extent of the mesenteric attachment. Since all degrees of this condition are possible, the demarcation between what constitutes the normal and what the abnormal is difficult to make. It is suggested that if the term "mobile cecum" is to have any clinical significance, its application be limited to a cecocolon which usually lies in its proper position but which potentially is subject to a process of rotation in the intact abdomen of the living person.

Little correlation can be demonstrated between vertical or horizontal (i. e., nonrotatory) mobility of the cecum and the incidence of clinical symptoms. Kantor and Schlechter,[4] in a series of 383 roentgen examinations, observed that in 10.4 per cent of their cases there was evidence of a cecum with a vertical range of movement of 2½ inches (6.35 cm.) or more, but they could not discover any association between this degree of mobility and the occurrence of headache, vomiting, pain in the lower part of the abdomen or constipation. Likewise, the demonstration in the cadaver that a cecum can be rotated and twisted has little clinical significance. In a series of 640 necropsies, Wandel[5] found that the cecum was mobile enough to allow "kinking, torsion and displacement" in 66 instances (10.3 per cent), and von Thun[6] felt that he could create volvulus of the cecum in 72 (21.3 per cent) of 338 cadavers; yet in each series, a history of symptoms which could be ascribed to the cecal anomaly was discovered only once. Many other authors have examined autopsy material to determine the frequency with which a mesentery persists on the right side of the colon, but usually without any attempt to employ uniform criteria or to establish any correlation with clinical symptoms. Table 1 lists some of the reported results.

From these figures it is obvious that slight mobility of the cccocolon is common. Far less frequent is the cecocolon sufficiently unattached to allow the occurrence of a spontaneous volvulus. In only 7 cases (1.1 per cent) in Wandel's[5] series did autopsy material show a mobility of the cecocolon as extensive as that present in 4 clinical cases of acute cecal volvulus. Other factors besides such a definite lack of fixation are, how-

4. Kantor, J. L., and Schlechter, S.: Colon Studies: VII. Variations in Fixation of the Ceco-Colon; Their Clinical Significance, Am. J. Roentgenol. **31**: 751, 1934.

5. Wandel, O.: Ueber Volvulus des Caecum und Colon ascendens, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **11**:39, 1903.

6. von Thun, cited by Jacobsen.[11]

ever, important in determining whether the mobile cecocolon will give rise to clinical symptoms or not. Volvulus will probably not occur unless some suitable fixed point is present about which the loose bowel can rotate. Further, volvulus may be prevented by adhesions, by intra-abdominal tension or by the position of the other viscera. The importance of these accessory factors is demonstrated by the relative infrequency with which acute cecal volvulus occurs. Sweet [7] found that in 520 cases of acute intestinal obstruction exclusive of external strangulated hernia, only 6 (1.15 per cent) were due to volvulus of the cecum. Other authors give somewhat higher figures (Pratt and Fallis,[8] 5 to 6 per cent; Leonard and Derow,[9] 3 per cent; Toprower,[10] 3.2 per cent; Jacobsen,[11] 15 per cent), but even if the highest of these figures is taken, it is clear that not every person with an unattached cecocolon suffers from clinical symptoms.

TABLE 1.—*Frequency with Which a Persisting Mesentery Is Demonstrated on the Right Side of the Colon in Autopsy Material*

Author	Number of Necropsies	Percentage of Cases in Which There Was a Persisting Mesentery
Harvey [1]	105 (infants)	13
Dreyer: Beitr. z. klin. Chir. **75**:113, 1911	105	67
Fallon: Boston M. & S. J. **169**:600, 1913	100	24
Treves, cited by Harvey [1]	100	26
Smith: Anat. Rec. **5**:549, 1911	982 (infants)	31

The frequency with which a mobile cecum gives rise to chronic symptoms is difficult to determine. A review of some of the case reports in the literature (table 2) indicates that about 47 per cent of the patients with acute cecal volvulus suffer from chronic symptoms before the acute attack occurs; but this figure is probably low, for a number of the reports neglected to mention any history previous to that of the acute episode.

In addition, some persons probably experience recurring and transitory volvulus of the cecocolon without ever suffering complete intestinal obstruction. Sweet [7] and Corner and Sargent [12] each reported a case

7. Sweet, R. H.: Volvulus of the Cecum, New England J. Med. **213**:287, 1935.

8. Pratt, J. P., and Fallis, L. S.: Volvulus of the Cecum and Ascending Colon, J. A. M. A. **89**:1225 (Oct. 8) 1927.

9. Leonard, E. D., and Derow, S.: Volvulus: A Study of Twenty-Two Cases, New England J. Med. **218**:388, 1938.

10. Toprower, G. S.: Zwei Fälle von Volvulus coeci, Wien. klin. Wchnschr. **46**:1417, 1932.

11. Jacobsen, H.: Volvulus du caecum, Acta chir. Scandinav. **56**:181, 1924.

12. Corner, E. M., and Sargent, P. W. G.: Volvulus of the Cecum, Ann. Surg. **41**:63, 1905.

in which operation was undertaken because the history strongly suggested chronically recurring cecal volvulus. In both instances, laparotomy demonstrated the rotated and twisted ascending colon. The following case report is that of another patient with chronically intermittent volvulus of the mobile cecum; it is of interest because the diagnosis was unequivocally established before operation.

REPORT OF A CASE

Personal History.—C. P., a white single woman of 20, entered the surgical service of the Massachusetts Memorial Hospitals on Jan. 26, 1941. She complained of intermittent attacks of pain in the lower part of the abdomen which began six years previously and had gradually increased in severity, frequency and duration.

TABLE 2.—*Frequency with Which Chronic Symptoms Precede an Acute Cecal Volvulus*

Author	Total Cases of Cecal Volvulus	Number of Cases in Which There Were Chronic Symptoms
Jacobsen [11]	5	6
Weinstein: Ann. Surg. **107**: 248, 1938	2	1
Pratt and Fallis [9] (included cases with malposition of the colon)	3	2
Farley and Konwaler: Am. J. Surg. **48**: 664, 1940	1	1
Wandel [8] (all but 5 of these cases were collected from the literature)	40	17
Toprower [10]	2	1
Homans: Arch. Surg. **3**: 395 (Sept.) 1921	3	3
Grace: Canad. M. A. J. **38**: 346, 1938	2	1
Corner and Sargent [12]	5	1
McGowan: Proc. Staff Meet., Mayo Clin. **11**: 337, 1936	1	1
Sweet [7]	7	3
Bundschuh: Beitr. z. klin. Chir. **85**: 58, 1913	1	1
Total	81	39(47%)

At first, the symptoms had consisted of crampy sensations localized in the right lower quadrant of the abdomen; but subsequently the pains involved the left lower quadrant as well and were accompanied by moderate distention of the lower part of the abdomen. Immediately preceding admission, the patient had suffered two attacks which were complicated by nausea and vomiting. Precipitating factors appeared to be physical exercise or the ingestion of a heavy meal. Relief was obtained by lying down, by applying hot water bags or by massive enemas. Appendectomy had been performed five years before admission but had not relieved the symptoms.

The patient presented also two additional gastrointestinal complaints. One of these consisted of mild "indigestion" appearing five to fifteen minutes after eating and characterized by a heavy epigastric sensation. The other, marked constipation, was so severe that at one period in her life, bowel movements occurred only once every ten days. No history of cardiovascular, urinary or neuromuscular abnormalities was elicited. The menses were irregular and painful but apparently had no connection with her chief complaint.

Familial History.—Two cousins of the patient had died of bowel stoppage; one in youth, the other in middle adult life.

Physical Examination.—The patient was of average weight and height. Except for mild tenderness throughout the abdomen, no abnormalities were revealed.

Laboratory Data.—The urine contained no sugar, albumin or abnormal elements in the sediment. The hemoglobin content was 95; the erythrocyte count was 4,800,000; the leukocyte count was 7,300. The differential leukocyte count was normal. The stools were brown, formed and negative to the guaiac test.

Roentgen Studies.—A gastrointestinal series of roentgenograms revealed no abnormalities of the stomach or the duodenum. Plates taken five and twenty-four hours after the ingestion of the barium sulfate meal showed the opaque material in the ascending colon, which presented a normal outline. A roentgenogram taken after the patient had been given an enema of barium sulfate demonstrated flatus in the small bowel and what appeared to be a dilated intestinal loop, partially obscuring the ascending colon (*A* in figure). After the patient had evacuated the bowel, the same abnormalities were visible but to a lesser degree. A study of the small bowel, with roentgenograms taken every hour for seven hours after the patient had taken barium sulfate by mouth, showed no abnormalities; and the ascending colon, which contained opaque material in the last three films, appeared normal in outline, size and position. The roentgenologic department, while recognizing that the films taken after giving the enema of barium sulfate were suggestive, did not feel an adequate interpretation could be given, especially since similar changes in the bowel could not be demonstrated in either the gastrointestinal series or the study of the small bowel.

Special Studies.—Since gastrointestinal roentgenograms had suggested that some intestinal abnormality was present but had not clarified the nature of this disorder, further diagnostic study was indicated. Ingelfinger and Abbott[13] showed that by employing two modifications of the Miller-Abbott method of small intestinal intubation,[14] specific information can often be obtained in cases in which the usual examinations yield questionable results. The first of these modifications consists of recording the small intestinal muscular activity, a method which was first used by Abbott and his collaborators[15] in studying the small bowel when obstructed and when under the influence of drugs. In the present case, a perfectly normal record of small intestinal activity was obtained. An unusual feature was encountered, however, when the patient was subjected to fluoroscopic examination after the record had indicated that the tip of the tube had entered the cecum. Instead of appearing in the right lower quadrant of the abdomen, as was anticipated, the tip of the tube was seen to lie in front of the third lumbar vertebra.

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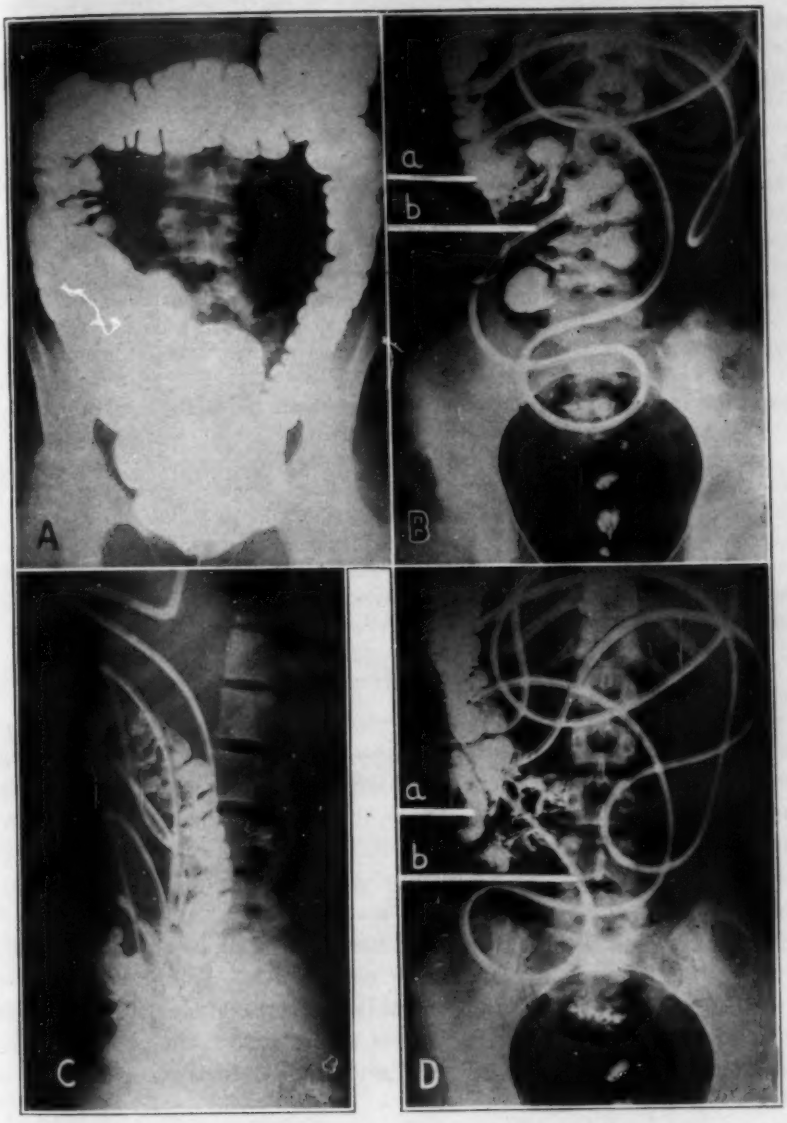
13. Ingelfinger, F. J., and Abbott, W. O.: Intubation Studies of the Human Small Intestine: XX. The Diagnostic Significance of Motor Disturbances, Am. J. Digest. Dis. **7**:468, 1940.

14. Miller, T. G., and Abbott, W. O.: Intestinal Intubation: A Practical Technique, Am. J. M. Sc. **187**:595, 1934.

15. Abbott, W. O., and Pendergrass, E. P.: Intubation Studies of the Human Small Intestine: V. The Motor Effects of Single Clinical Doses of Morphine Sulphate in Normal Subjects, Am. J. Roentgenol. **35**:289, 1936. Abbott, W. O.; Zetzel, L., and Glenn, P. M.: Observations on the Motor Activity of the Obstructed Small Intestine Made During the Course of Treatment by Intubation, Am. J. M. Sc. **195**:279, 1938.



In *A*, the colon has been outlined by an enema of barium sulfate. Flatus shadows appear in the small intestinal loops. In the right lower quadrant of the abdomen a large dilated loop of bowel is filled with the opaque medium. In *B*, barium sulfate outlines the cecocolon, which is displaced medially and sharply angulated at *a*. The tip of the tube lies in the cecum, just beyond the ileocecal valve. The distal portion of the tube (*b*) lies in the terminal part of the ileum, which enters the cecum from the wrong direction. *C*, a lateral view showing the angulation in the ascending colon. In *D*, the cecocolon is now in its usual position, but the angulation at *a* is more acute. The terminal part of the ileum (*b*) now enters the cecum in the usual manner.

At this point, the second modification of the Miller-Abbott procedure, a modification originally described by Abbott and Johnston,[16] was employed. A thin suspension of barium sulfate was injected through the tube in order to delineate that part of the intestine which contained the tip. By means of the fluoroscope, the injected opaque substance was seen to flow in two directions, orad and caudad, but it did not regurgitate backward along the tube. A roentgenogram taken at the same time (*B* in figure) showed that the terminal part of the ileum was entering the cecum from the wrong direction (i. e., from right to left) and that the cecocolon was both displaced and sharply angulated. The angulation is more noticeable in *C* in the figure. After the patient's position on the fluoroscopic table was changed, the ileum and the cecocolon started to move without any further manipulation by the operator and assumed the position shown in *D* in the figure. The ileum was now entering the cecum in the usual manner (i. e., from left to right), and the cecocolon lay in its normal position, although the angulation in the ascending colon was more acute. These roentgenograms offer definite proof that the cecocolon in this patient rotated through an arc of 180 degrees under the ordinary stimuli of bodily movement and gravity.

At operation, the cecocolon was found to be freely movable, and both the ascending and the descending colon possessed long mesenteric attachments. In an attempt to prevent any further episodes of volvulus, the cecocolon was fixed to the right posterior parietal wall. At the time of writing, the patient has not suffered any further attacks of pain in the lower part of the abdomen, distention, nausea and vomiting since operation. Her complaint of "indigestion" has so far persisted, but the constipation is much less marked and easily controlled with liquid petrolatum.

COMMENT

This case offers definite demonstration of two phenomena which heretofore have been supported only by inference based on observations made at the operating or the autopsy table. In the first place, the studies carried out with the aid of the Miller-Abbott tube demonstrate that when the proper anatomic conditions obtain, the cecocolon can rotate through an angle of 180 degrees in the intact abdomen of a living person and that the stimulus for this rotation need be no more than a simple bodily movement. It is claimed that a torsion of more than 180 degrees is necessary to produce the signs and symptoms of volvulus. With regard to the present case, this contention is probably correct, for when the cecocolon had undergone the twist of 180 degrees (*B* in figure), the patient experienced no symptoms, and a roentgenogram showed no evidence of intestinal obstruction.

In the second place, this case demonstrates that a cecocolon of enough mobility to rotate through an arc of more than 180 degrees can at times be subject to further torsion; when this happens, typical, but usually transitory, cecal volvulus is produced. In the figure, *B* shows the unmistakable characteristics of intestinal obstruction: a dilated intestinal loop and the accumulation of flatus in the small bowel. Hence, there

16. Abbott, W. O., and Johnston, C. G.: Intubation Studies of the Human Small Intestine: X. A Non-Surgical Method of Treating, Localizing and Diagnosing the Nature of Obstructive Lesions, Surg., Gynec. & Obst. **66**:691, 1938.

can be little doubt that the abdominal pain and distention in this case were occasioned by intermittent and partial volvulus of the mobile cecocolon.

As stated previously, a mobile cecocolon with intermittent volvulus is a rare condition. Nevertheless, it is important to make the diagnosis whenever possible, for surgical fixation of the ascending colon will usually alleviate the symptoms of intermittent intestinal obstruction. Even more important, fixation should prevent the occurrence of a cecal volvulus which fails to reduce itself and which must be treated as an acute and dangerous surgical emergency.

As is true in the present case, the history of patients with chronic cecal volvulus is characteristic. Usually the person is young and active. The symptoms are those of intermittent intestinal obstruction: crampy pains most frequently involving the lower part of the abdomen, distention and, occasionally, nausea and vomiting. These symptoms are usually precipitated by the ingestion of a heavy meal or by physical exercise, persist anywhere from one-half to four hours and then usually subside spontaneously. Almost invariably, the patient has severe constipation, and frequently a fruitless appendectomy has been performed.

If a patient with such a history is encountered and if the usual clinical and roentgen studies are negative or inconclusive, special studies similar to those used in the present case are indicated. It is not maintained that in every case mobile cecocolon with a tendency toward intermittent volvulus can be diagnosed, but if the Miller-Abbott method of intestinal intubation and its modifications are used as diagnostic procedures, the chances of recognizing such an obscure condition as a mobile cecocolon are enhanced.

SUMMARY

If the term mobile cecum is to have any clinical significance, its application should be limited to a cecocolon which usually lies in its proper position but which potentially is subject to a process of rotation in the intact abdomen of the living person.

Mobile cecocolon with a tendency toward intermittent volvulus is a rare condition. About one half of the patients who come to operation because of acute cecal volvulus suffer from chronic symptoms previous to the acute attack.

Roentgenograms of a patient whose case is presented demonstrate that in the intact abdomen of this living person: (1) the cecocolon could easily rotate through an angle of 180 degrees and (2) transient intestinal obstruction due to cecal volvulus could occur.

By using two modifications of the Miller-Abbott method of small intestinal intubation, the possibilities of diagnosing mobile cecocolon are increased.

Dr. Lois Miller of the roentgenologic department and Dr. Hollis Albright of the surgical department helped in the diagnosis and in the treatment of this patient.

LIPOSARCOMA

REPORT OF NINE CASES

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AND
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HINES, ILL.

A survey of the literature indicates that liposarcoma is a neoplasm of extremely rare occurrence. Virchow [1] (1857) is credited with the first accurate histologic study of this tumor, and in 1939, Lingley [2] reported a case of liposarcoma which was noted as the seventy-second one to be recorded.

Recently, however, there has arisen the impression that these figures do not represent a true estimate of the clinical frequency of liposarcoma. The extremely variable microscopic features shown by liposarcoma (stressed by Geschickter [3] and others) may have occasioned the classification of certain of these tumors as endothelial, carcinomatous or xanthomatous neoplasms. At times, liposarcoma has undoubtedly been mistakenly diagnosed as fibrosarcoma.

From Jan. 1, 1931, to Jan. 1, 1941, approximately 16,000 patients with tumor were admitted to the Veterans Administration Facility, and from this group a diagnosis of liposarcoma was made in 9 instances. This seems to suggest a somewhat higher frequency than is indicated by the paucity of reports in the literature.

REPORT OF CASES

CASE 1.—Q. E. K., a white barber aged 68, was admitted to the hospital on April 11, 1939. The familial history was negative. The illness presented dated from Jan. 1, 1939; at that time the patient noted a lump under the skin just below the right scapula. It was small, hard and freely movable. It grew rapidly, reaching

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From the Tumor Service and the Pathological Laboratory of the Veterans Administration Facility.

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1. Virchow, cited by Geschickter.[3]

2. Lingley, J. R.: Liposarcoma: Case Report, Am. J. Roentgenol. **41**:851-854 (May) 1939.

3. Geschickter, C. F.: Lipoid Tumors, Am. J. Cancer **21**:617-641 (July) 1934.

a diameter of 6 inches (15.2 cm.) in a few weeks, and protruded about 4 inches (10.2 cm.) above the surface. The family physician incised the tumor but did not attempt removal.

The site of the incision broke down, and the tumor assumed a cauliflower-like growth. From the time the tumor was noted until admission, the patient lost 30 pounds (13.6 Kg.).

On admission the tumor was 8 inches (20.3 cm.) in diameter, not painful and firmly attached to the underlying tissues; the surface was fungating. There was no demonstrable adenopathy. Roentgen examination of the chest revealed nothing of interest. Kahn and Wassermann tests were negative. Urinalysis was negative.

Wide excision of the growth was done with a Bovie knife and included part of the underlying fascia and the latissimus dorsi muscle. Punch grafts were applied to the surface of the wound. There was complete healing at the time of discharge, July 7, and the patient appeared to be well. He had gained 4 pounds (1.8 Kg.).

On November 1 the patient was readmitted with a small lump 1 cm. in diameter in the scar. This was excised and found to be a keloid.

Examination on Aug. 15, 1940 showed the patient free from evidence of metastasis or recurrence. He is well at the time of writing.

Gross Description.—The tumor measured 10 by 8 by 8 cm. The surrounding skin and soft tissues were attached. The surface was red with a cauliflower appearance. The cut section was firm and glistening and yellowish white. The tumor was not encapsulated. It had not invaded the surrounding soft tissues.

Microscopic Description.—The cells were oval and polyhedral in shape and showed great variation in size. In some, the cytoplasm was vacuolated. The vacuoles stained with sudan III and were doubly refractive. The nuclei were eccentrically placed and for the most part were hyperchromatic. There was some variation in the chromatin content of the nuclei, and they varied markedly in size and shape. Mitoses were frequent. The diagnosis was liposarcoma.

Case 2.—H. S., a white bank clerk aged 44, was admitted to the hospital on Feb. 2, 1938. The past history revealed the usual diseases of childhood. Venereal diseases were denied.

The illness dated from the patient's discovery of a mass in the upper part of the abdomen three months earlier. The tumor was not painful. Since the discovery of the tumor, the patient suffered frequent spells of dizziness and had fainted on a number of occasions; he had lost 14 pounds (6.4 Kg.).

Examination revealed a large mass in the right upper quadrant of the abdomen, extending to the left of the midline and downward to the level of the crest of the ilium. The tumor presented no definite outline and was not tender; it moved with respiration.

Pyelograms showed no dye in the right kidney. Preoperative irradiation was given with no response. Roentgen examination of the gastrointestinal tract, the gallbladder and the skull revealed no abnormalities.

Operation on March 17 revealed a large retroperitoneal tumor. This mass involved the blood supply to the right kidney but did not invade the kidney. The kidney was removed. The postoperative recovery was good. The patient gained

12 pounds (5.4 Kg.) and was discharged on June 2 with no demonstrable evidence of metastasis or recurrence. Extensive postoperative irradiation was given.

The patient went back to work and continued to gain weight.

At the end of a year the abdomen began to enlarge; ascites developed, and edema of the lower extremities was noted. The patient lost weight, and the course was steadily downhill, until death occurred on July 25, 1940.

Gross Description.—The resected tumor weighed 5,000 Gm. It was grayish white, firm, friable and vascular. The mass was not well encapsulated but was completely removed.

Microscopic Description.—The cells were round, polyhedral and spindle shaped. They were vacuolated. The nuclei were hyperchromatic for the most part, but the chromatin content varied in amount. Many mitoses were noted. The stroma was scanty. The growth was well vascularized. The diagnosis was liposarcoma.

Autopsy.—Autopsy revealed a massive lesion; the entire right lobe of the liver was replaced by tumor, the center of which had broken down. There was an extensive retroperitoneal tumor mass which was of identical histologic structure as the original tumor. The structure of the tumor of the liver also was identical.

Case 3.—E. O. C., a white laborer aged 52, was admitted to the hospital on Dec. 13, 1938. The familial and personal histories revealed nothing of interest. The illness dated from 1930, when three masses were excised from the patient's left hip. The growth recurred in 1932 and was excised; a later recurrence was excised in 1934. No operation records or pathologist's report were available.

At the time of admission to the hospital, the patient complained of tumor masses in the left buttock; these had begun to grow about a year previously.

Examination revealed a well developed, rather obese man in good general physical condition. Three tumor masses were noted in the left buttock, firmly adherent to surrounding soft tissue and old excision scars. Roentgen examination of the chest and the skeleton found no evidence of metastasis.

Three masses were widely excised with a Bovie knife on Jan. 27, 1939. The three masses were 7 to 10 cm. in diameter and adherent to scars and surrounding soft structures. The masses were partially encapsulated, but in places they apparently invaded the muscle.

Gross Description.—The tumor tissue was firm in consistency and was friable. Grossly, the tumor did not appear to be fat.

Microscopic Description.—Many large, mature fat cells were seen, along with many groups of immature large light-staining cells with firmly granular cytoplasm. The nuclei were round, hyperchromatic and eccentrically placed. Many of the cells had two or three nuclei. No mitoses were present. The diagnosis was liposarcoma.

The patient was discharged in good condition on February 24. At the time of writing, there is no evidence of recurrence.

Case 4.—J. C. S., a white man aged 38, was admitted to the hospital on Dec. 27, 1934. His father had died of cancer; otherwise, the familial history revealed nothing of note. The personal history was not important.

Fifteen years previously, the patient had noted a small freely movable lump on the right lateral wall of the chest, just below the axilla. Two years before admission, the lump began to grow; it was excised six months before admission.

The patient stated that the excised tumor weighed 3 pounds (1.3 Kg.) and was diagnosed as Hodgkin's disease. The slide of this tumor was reviewed at the time of admission, and a diagnosis of liposarcoma was made.

Large discrete masses were noted in the right axillary and cervical regions. The original tumor and these axillary and cervical masses were subjected to intensive irradiation, with no effect on the size. A sinus developed in the axillary region and drained profusely. Surgical excision of this sinus was done, and death resulted from massive postoperative hemorrhage from the operative wound. There was no autopsy.

Fig. 1. (case 4).—Photograph showing massive fungating ulcerative tumor of the wall of the chest prior to surgical excision.

CASE 5.—H. D. B., a white farmer aged 49, was admitted to the hospital on April 4, 1940, from Veterans Administration Facility, Fayetteville, Ark., with a diagnosis of sarcoma of the right thigh. The patient stated that he had watched the tumor grow from the size of a bean to that of a watermelon during the past eight years. At first, he was able to pick up the nodule and roll it under the skin. In four years it grew to the size of a walnut. In September 1934, it was a little larger than a hen's egg. The growth was steady but slow, until the last eighteen months before admission, during which it grew rapidly to massive proportions.

An attempt had been made by the family physician to remove the growth, but he had encountered excessive bleeding and closed the wound. On admission to this hospital, the patient was in fairly good general physical condition; he was well nourished and had lost little weight. He was confined to bed because of the

disability occasioned by the tumor occupying the entire anteromedial aspect of the right thigh. The mass extended from the knee to the inguinal ligament and beneath the ligament retroperitoneally, occupying the entire right lower quadrant of the abdomen. This was interpreted as extension of the tumor to the abdominal and retroperitoneal regions.

Although only a few rales were heard at the base of the right lung, roentgenograms showed a 4 cm. spherical shadow in the right cardiophrenic angle; this was considered indicative of metastatis. Roentgenograms of the thigh showed no involvement of the femur.

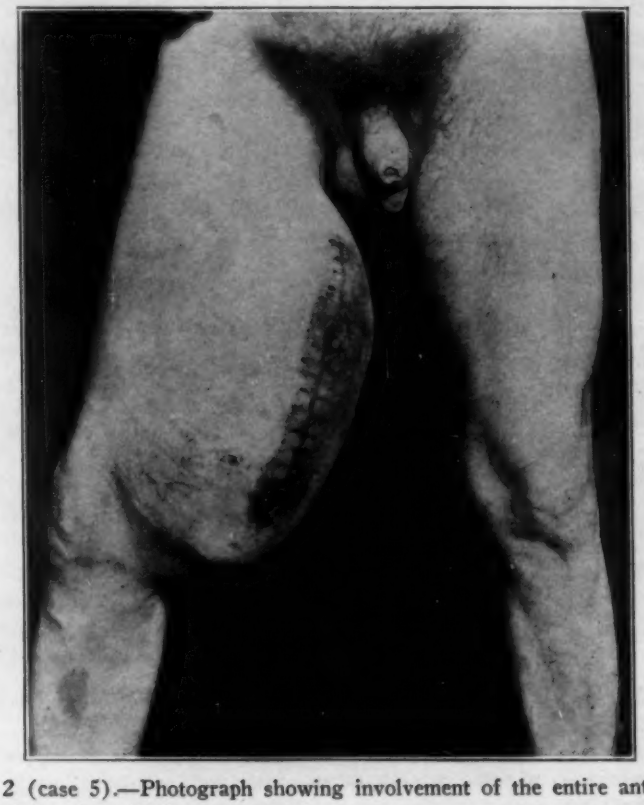

Fig. 2 (case 5).—Photograph showing involvement of the entire anteromedial portion of the right thigh.

The tumor was considered inoperable. Biopsy was done.

Biopsy.—The section showed numerous irregular cells, most of which tended to be spindle shaped. The nuclei were hyperchromatic, round or slightly elongated and eccentrically placed. The cytoplasm was granular and vacuolated. Occasional mitoses were seen. A few giant cells were noted.

At his request, the patient was allowed to return home.

CASE 6.—W. D. S., a white man aged 45, a farmer and barber by profession, entered the hospital on March 27, 1940. The familial and personal histories presented nothing of interest. Illness had been noted three months before admission

with the onset of pain in the upper part of the abdomen and vomiting after meals. During this time, the patient lost 40 pounds (18.1 Kg.).

Examination revealed an emaciated man with the appearance of chronic illness. A large hard tumor was palpated in the epigastrium and the upper left quadrant of the abdomen. The liver and the spleen were not palpable.

Rectal examination revealed nothing of note. It was impossible to make a gastrointestinal roentgen series owing to incessant vomiting. A diagnosis of probable tumor of the stomach was made, and exploratory laparotomy was done.

The operation revealed a large orange-colored nodular tumor measuring 8 by 15 cm. and located in the upper two thirds of the mesentery of the jejunum.

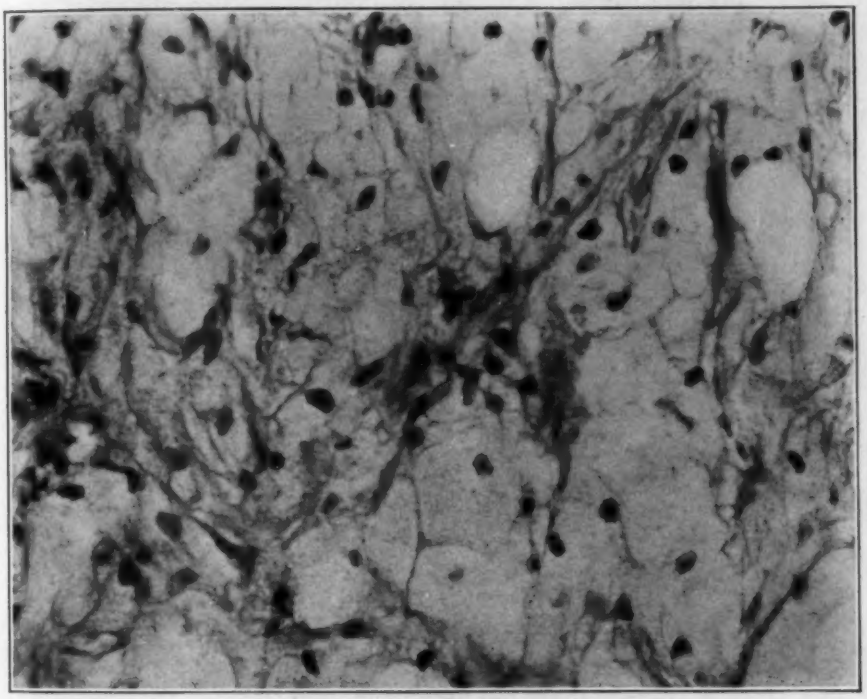

Fig. 3 (case 3).—Photomicrograph (× 286) showing growth consisting of large mature fat cells with eccentrically placed nuclei. Small irregular foamy cells are also present.

Material for biopsy was taken, and the abdomen was closed, the tumor being judged inoperable. The tissue removed was firm in consistency and yellowish white in color.

Biopsy.—Mature fat cells and aggregations of large and small granular cells were seen. These cells had small hyperchromatic nuclei. Numerous vacuoles were seen which took the fat stain. Occasional mitoses were seen. The diagnosis was liposarcoma.

The patient was given postoperative irradiation with no evident diminution in the size of the tumor.

At the time of writing, the patient is ambulant, but the tumor shows constant increase in size, and the outlook is hopeless.

CASE 7.—J. P., a white man aged 39, was admitted to the hospital on April 7, 1939. The familial and personal histories revealed nothing of note.

About one year previously, the patient had noted that the abdomen was enlarging. He also noted a loss of weight and strength. He consulted the family physician who advised him that he had an abdominal tumor and advised an operation. This was done, and the physician reported the presence of a retroperitoneal tumor the size of a football, which he considered inoperable. Biopsy was done and the diagnosis of fibrosarcoma made. The tumor was yellowish and nodular. The regional lymph nodes were invaded. After recovery from this operation, the patient was transferred to this hospital for further treatment. Another exploratory operation

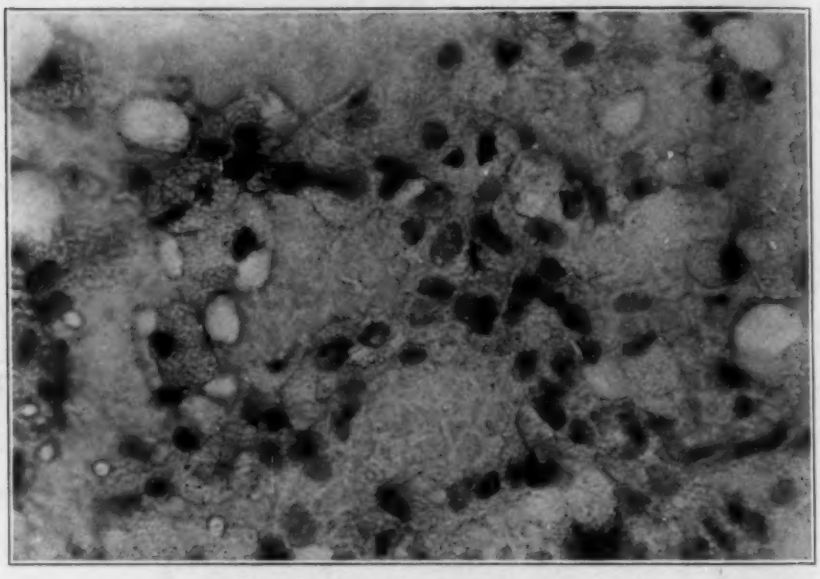

Fig. 4 (case 1).—Photomicrograph of high power magnification showing large cells containing fat. The section was stained with sudan III.

was done, and a retroperitoneal tumor, weighing 15 pounds (6.8 Kg.), was removed. The mass was horseshoe shaped, lying on each side of the spine and attached at the midline at the level of the duodenum. Small remnants of the tumor and large infiltrated lymph nodes could not be removed.

The patient recovered rapidly and gained weight. He was discharged June 19. Roentgen examination showed no evidence of metastasis. The patient is well at the time of writing.

Gross Description.—The tumor weighed 15 pounds (6.8 Kg.). It was nodular, firm and grayish white. It had a firm capsule.

Microscopic Description.—Histologic examination revealed large mature fat cells and masses of polygonal and spindle-shaped cells with granular cytoplasm containing vacuoles. Some of these cells had vesicular nuclei, and others had small hyperchromatic nuclei. A few mitoses were seen. A small number of

lymphocytes, eosinophils and foreign body giant cells were noted. The diagnosis was liposarcoma of a low degree of malignancy.

CASE 8.—A. M. R., a white farmer aged 45, was admitted to the hospital on April 10, 1936. The familial and personal histories revealed nothing of interest.

About fifteen years previously, the patient had noted a small lump in the right thigh. About eighteen months prior to admission, the lump began to grow rapidly. At the Veterans Administration Facility, Indianapolis, the tumor was removed from the upper part of the right popliteal space. It was 3 inches (7.6 cm.) in diameter, grayish white and homogeneous. It was encapsulated.

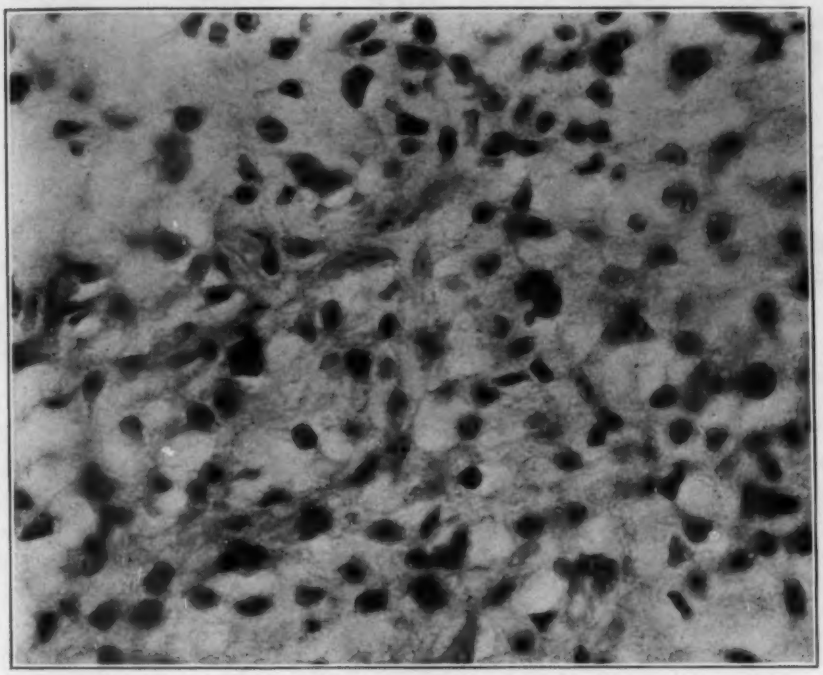

Fig. 5 (case 8).—Photomicrograph (× 286) showing moderately cellular tumor. The cytoplasm is granular and vacuolated; the nuclei are dark and eccentrically situated.

Microscopic Examination.—Histologic examination revealed a moderately cellular growth made up of spindle-shaped and oval-shaped cells. In the oval cells, the nuclei were small and hyperchromatic, often eccentrically placed. Both types of cells were granular and vacuolated. The vacuoles in some instances pushed the nuclei to one side. An occasional mitosis was noted. The diagnosis was liposarcoma of a low degree of malignancy.

This patient received no irradiation. Roentgen examination of the chest and the bones showed no evidence of metastasis.

The patient is well with no evidence of recurrence at the time of writing.

CASE 9.—J. L. W., a white salesman aged 45, was admitted to the hospital on July 20, 1936. The familial and personal histories presented nothing of note. Two

months prior to admission, the patient noted a nodule in the left hip. It grew progressively larger.

Shortly after the patient was admitted, the tumor was resected from the left gluteal region.

Gross Description.—The resected tumor was 15 cm. in diameter; it was grayish yellow and white, with small areas of hemorrhage and necrosis. It had a thin capsule. The surface was glistening and mucoid. There was evidence of invasion of the soft tissues.

Microscopic Examination.—Histologic examination revealed cells of irregular size and shape—spindle shaped, round and polygonal. Occasional cells were

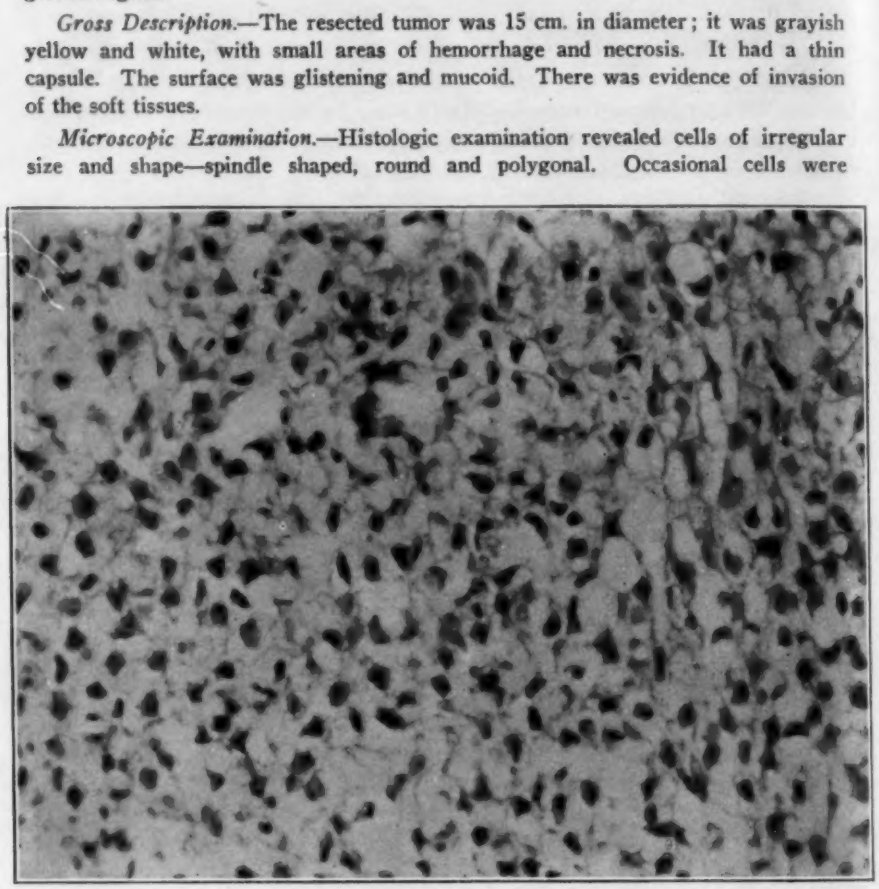

Fig. 6 (case 9).—Photomicrograph (× 286) showing vacuolated cells and dark nuclei; the latter are eccentrically placed and vary in size and shape.

recognized as adult fat cells. The majority of the cells were granular with reticular nuclei. Many cells contained vacuoles which had pushed the nuclei aside. The smaller cells had eccentrically placed small hyperchromatic nuclei and also showed vacuoles. An occasional mitotic figure was seen. There were extensive areas of myxomatous degeneration. The diagnosis was liposarcoma of a low degree of malignancy.

Roentgen examination of the chest and the bones showed no evidence of metastasis.

Intensive postoperative irradiation was given. The patient is well with no evidence of recurrence at the time of writing.

COMMENT

Location.—The most frequent site of origin for liposarcoma seems to be in the soft tissues of the lower extremity; the second most frequent, the retroperitoneal space. In a series of 12 cases of liposarcoma reported by Geschickter, in 5, the tumor was on the thigh or the leg; in 3, in the breast; in 2, in the forearm and the arm; in 1, on the back, and in 1, in the thorax. In a series of 51 cases collected by Robertson,[4] in 42 per cent it was in the thigh or the lower part of the limb.

Various other sites of origin include the mediastinum,[5] the vulva[6] and bone.[7]

The following sites of origin were noted in the cases described in this report: the gluteal region and the thigh in 4 cases; the retroperitoneal region in 3 cases; the right lateral wall of the chest just below the axilla in 1 case; the right scapular region in 1 case.

Clinical Course and Prognosis.—The clinical history of liposarcoma almost invariably includes the discovery by the patient or the physician of a mass or lump. The tumor may grow slowly over a period of years, or the rate of growth may be extremely rapid. One patient in our series (case 5) observed a tumor of the right thigh grow from the size of a bean to that of a watermelon over a period of eight years. Another patient (case 1) observed an increase in a small tumor of the scapular region to a diameter of 6 inches (15.2 cm.) with a protrusion of 4 inches (10.2 cm.) above the skin surface in six weeks. In case 8, the tumor was known to be present fifteen years before it exhibited growth.

When the tumor is retroperitoneal, the usual signs and symptoms of neoplasms of this region are encountered: enlargement of the abdomen and derangement of functions in the various abdominal and pelvic organs caused by compression and encroachment of the expanding mass.

When the tumor exhibits signs of rapid growth and activity, the usual clinical signs of malignancy ensue.

Recurrence and metastasis are the rule with liposarcoma. These may be encountered early or late. Lingley noted in this regard:

> All authors are agreed on the marked degree of malignancy of this tumor. The mass is usually encapsulated and, if simply shelled out or excised, it invariably

4. Robertson, H. E.: Lipoma Myxomatodes, J. M. Research **35**:131-146, 1916.

5. Perkins, C. W., and Bowers, R. F.: Liposarcoma of Mediastinum and Lung, Am. J. Roentgenol. **42**:341-344 (Sept.) 1939.

6. Taussig, F. J.: Liposarcoma of the Vulva, Am. J. Obst. & Gynec. **33**:1017-1026 (June) 1937.

7. Stewart, F. W.: Primary Liposarcoma of Bone, Am. J. Path. **7**:87-93 (March) 1931.

recurs locally. Even fairly wide excision may be followed by local recurrence and metastasis. In Geschickter's series of 12 cases the tumor recurred after excision in every case but one which was only recently observed. No case was reported cured.

Geschickter found that the duration of symptoms from the first complaint until metastasis was known to occur averaged ten years in his series.

In the case reported by Taussig, a lump located in the left labium majus pudendi grew large in six months. It was enucleated, and the diagnosis of liposarcoma was made. It recurred in two weeks and at the end of six weeks it was 4 by 2.5 cm. in size. One-sided vulvectomy was done. Two months later widespread metastasis was evident in the lungs and the bones. Death ensued after six months.

Fender [8] reported a case in which a five year period elapsed after extirpation of a liposarcoma of the leg. At this time an intracranial metastasis was removed by operation, and at the time of this report the patient showed evidence of recurrence of the intracranial tumor.

Fender noted that "the few cases available for study seem to indicate that these tumors grow slowly, are radiosensitive, metastasize late and show a tendency to metastasize to the cranium." Dr. F. B. Mallory reviewed the sections of the original tumor of the leg in Fender's case and pronounced this tumor to be identical with the cranial tumor, concurring in the diagnosis of late intracranial metastasis from a primary liposarcoma of the leg.

In our series of 9 cases of liposarcoma, the outcome at the time of writing is as follows:

Case 1.—Patient is well with no signs of metastasis or recurrence after twenty months.

Case 2.—Recurrence occurred after one year; death, two months later.

Case 3.—There is no evidence of metastasis or recurrence after two years.

Case 4.—Recurrence occurred after six months; death followed massive hemorrhage subsequent to removal of recurrence by operation.

Case 5.—An enormous tumor of the right thigh, inoperable when seen at this hospital, is present; there is roentgen evidence of metastatic growth under the right cardiophrenic angle.

Case 6.—The retroperitoneal tumor, inoperable at exploratory operation, is growing; the outlook is hopeless.

Case 7.—Good postoperative recovery followed removal of the retroperitoneal tumor. Small remnants of the tumor and the infiltrated lymph nodes could not be removed. The patient is well after twenty months.

Case 8.—The patient is well with no evidence of metastasis or recurrence five years after removal of the tumor from the right popliteal space.

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8. Fender, F. A.: Liposarcoma: Case with Intracranial Metastases, Am. J. Path. **9**:909-914 (Nov.) 1933.

Case 9.—The patient is well with no evidence of metastasis or recurrence four years and nine months after removal of the tumor from the left gluteal region.

Liposarcoma has been listed by certain authors as a radiosensitive tumor. In certain of our cases, irradiation was used with no demonstrable favorable effect.

Diagnosis.—The diagnosis of liposarcoma is naturally made by histologic examination. In case 4 of our series, the original tumor examined elsewhere was misdiagnosed as Hodgkin's disease. A review of the slides and a study of the recurrence showed liposarcoma.

Castleman, in discussing Lingley's report, said regarding the histologic diagnosis of liposarcoma:

. . . Throughout the tumor all shapes of fat cells from small embryonic fat cells to large adult fat cells could be found, a fact that definitely rules out fatty degeneration of fibrosarcoma, a condition that is sometimes erroneously called liposarcoma histologically.

Pathologic Description.—It is frequently noted that liposarcoma tends to be well encapsulated and may shell out easily at operation. Despite this fact, it often recurs locally and metastasizes. Recurrence and metastasis, however, frequently follow wide excision.

Fender described the histologic picture in his case of liposarcoma as follows: "None of the cells were differentiated into adult fat cells, but they had granular cytoplasm, eccentric nuclei and alveolar arrangement which are considered characteristic."

Perkins and Bowers' well encapsulated specimen of liposarcoma was microscopically extremely cellular. They described it histologically as follows:

. . . [The] basic architecture might be said to resemble that found in liver, in that there were small lobules with a central vessel about which the neoplastic elements were growing. Each of these in turn presented a thin capsule-like structure of cellular fibrous tissue, areas of which presented hyaline degeneration. . . . The cells were small, loosely arranged, with but little cytoplasm. Many of the nuclei were hyperchromatic, and were of the wheel-like type, resembling those of plasma cells. Others, however, had more than a mere rim of cytoplasm; their nuclei were larger but did not stain deeply and suggested an endothelial origin. In attempting further to identify their origin, a section stained with sudan III showed that they almost invariably contained tiny fat granules. Because of their primitive appearance, and the large amount of fat, this tumor was considered lipogenic. Diagnosis was liposarcoma. . . .

In the case reported by Taussig, sections of the tumor were sent to Dr. James Ewing for study and confirmation of the diagnosis. His microscopic description of this liposarcoma was as follows:

Sections of the tumor stained with hematoxylin and eosin show a moderately rich cellular neoplasm separated into smaller and larger masses of fine and coarse bands of fibrous tissue. The tumor cells are oval to spindle in shape and vary mark-

edly in size; the nucleus is small, and the cytoplasmic structure contains fat globules of varying size and number. The cytoplasm is finely granular. These cells represent varying stages in the development of fat cells. The reticulum of the tumor demonstrated by the Foot modification of the Bielschowsky silver impregnation method is abundant in quantity and mainly in the form of a plexus surrounding each cell, the whole forming a network. The intracellular fat was demonstrable in the frozen section, stained with sudan III. The lymph nodes present a moderate hyperplasia, with no evidence of tumor cells.

Geschickter summarized the histologic picture of liposarcoma thus:

Liposarcoma shows extremely variable microscopic features. The predominating malignant tissue either resembles a fascial sarcoma with compact spindle cells or shows numerous immense tumor giant cells with degenerating nuclei and a large amount of foamy cytoplasm. Surrounding these malignant areas are islands of embryonic fat, adult fat, and myxomatous-like stroma. A small cell resembling a plasma cell or fetal cartilage cell is often seen. Whether it is a forerunner of the larger foam cell is not certain.

In our series of 9 cases of liposarcoma, the neoplasms were moderately cellular. The cells for the most part were round to spindle shaped and showed marked variation in size. The nuclei, as a rule, were small, frequently hyperchromatic and often eccentrically placed. The cytoplasm was finely granular and showed vacuoles of varying sizes. In some instances the vacuoles appeared to have displaced the nucleus toward the edge of the cell. As a rule, mitoses were few; mitotic figures were more abundant in the highly anaplastic metastasizing tumors. The stroma consisted of well vascularized fibrous connective tissue dividing the growth into cell aggregations of various sizes. The appearance of many of the smaller cells suggested embryonic fat. The presence of fat in the cells was demonstrated by sudan III or sudan IV stain.

SUMMARY

Nine cases of liposarcoma are described. These were encountered in the examination and treatment of 16,000 patients with tumor.

It is suggested that the clinical frequency of liposarcoma may be greater than the few cases reported in the literature would indicate.

INTERVAL INTRACRANIAL HEMORRHAGE: ITS DIAGNOSIS AND MANAGEMENT

ANALYSIS OF TWENTY-FIVE CASES

EMIL SELETZ, M.D.
LOS ANGELES

Since the vast majority of head injuries are of necessity treated by the industrial surgeon, this paper dealing with the diagnosis and the management of the only real surgical emergency among head injuries—the interval or delayed intracranial hemorrhage—should be of interest to him.

Interval hemorrhage is delayed intracranial bleeding that develops in either the extradural or the subdural space after an injury to the head. The injury may be slight; usually it is of sufficient severity to produce momentary unconsciousness. I have seen 4 professional boxers with interval hemorrhage after they had received a knockout blow in the ring. Twenty-two of the patients in this series of 25 suffered only a minor injury. Eleven had no period of unconsciousness.

The typical interval hemorrhage involves the middle meningeal artery. The sequence of events in this type of bleeding is as follows: The patient receiving a blow to the head, usually after a momentary period of unconsciousness, gets up and goes about his usual duties. During the injury, the middle meningeal artery has been torn. Within one or two hours, the patient complains of headache and often will place his hand over the region of the developing hemorrhage. Because of its location outside the dura, the bleeding artery produces an accumulation of blood between the dura and the cranial vault, and this stripping away of the dura from its attachment to the vault produces the pain. As the dura is being separated from the inner surface of the skull, other small branches of the meningeal artery are torn, and in this way the hemorrhage grows in size. This process within a few hours results in the accumulation of considerable tumor of blood, with resultant increase in intracranial pressure as well as pressure on the motor cortex of the brain. This relatively sudden increase in intracranial pressure produces gradually increasing drowsiness, stupor and, finally, coma, with slowing of the pulse and the respirations and contralateral motor weakness and perhaps paralysis. Frequently these

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symptoms are ushered in by a convulsion. Because of the anatomic location of the hemorrhage, pressure is exerted first in the face, then the arm area of the motor cortex; the convulsion begins in the face and the arm, and the paralysis develops in the same sequence, finally involving the lower extremity.[1]

During the development of the acute intracranial pressure there is a rise in the systolic blood pressure, while the diastolic remains relatively unchanged; this gives rise to a high pulse pressure with a characteristic full volume pulse. I have often seen blood pressures of 150 systolic and 60 diastolic or 180 systolic and 60 diastolic, giving a pulse pressure of 90 to 100. Spinal fluid findings show elevated

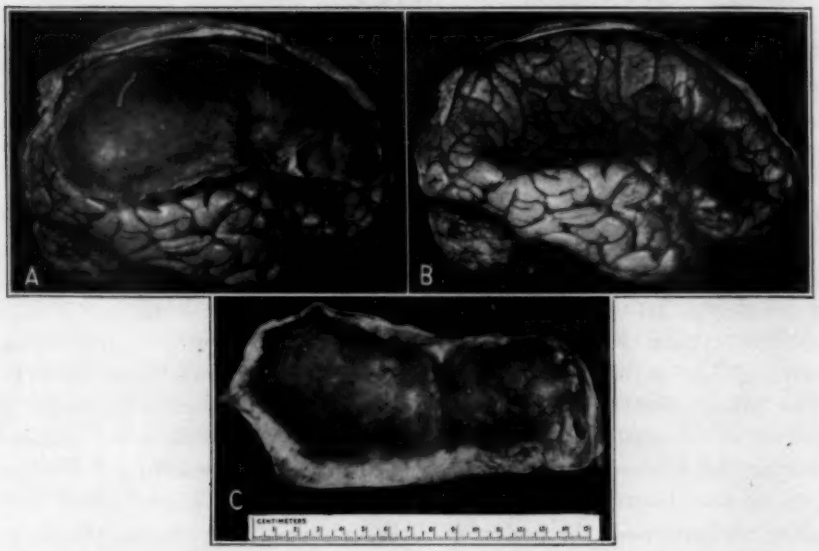

Fig. 1.—*A*, photograph of the brain at autopsy showing an encapsulated subdural hematoma; *B*, the hematoma has been removed, showing the depression of the cortex; *C*, the encapsulated hematoma.

pressure; the fluid is usually clear. Spinal punctures are dangerous in a case of suspected extradural hematoma [2] and are of little or no value in diagnosis other than to reveal a high intracranial pressure.

When the patient is deeply comatose, the breathing becomes deep and slow, with long, drawn out inspirations and a puffing out of the cheeks on expiration. This blowing type of respiration is much like that

1. Dandy, W. E.: Subdural Hematoma, Subdural Hydroma, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1932, vol. 12, pp. 295-309.

2. Extradural hematoma is synonymous with middle meningeal hemorrhage.

seen in a patient just entering the surgical stage of anesthesia induced with ether. I have never observed this type of respiration in any other type of craniocerebral injury. This characteristic pulse and blowing respiration has in my experience been a valuable aid in the diagnosis of middle meningeal hemorrhage, especially in those instances in which the history was inadequate. The blowing respiration and the full volume pulse were present in 10 of the 25 patients; all 10 were in deep coma.

By far the most important single symptom of progressive intracranial bleeding is a deepening coma.[3] Every patient with a history of head injury, who several hours later goes into a coma from which he cannot be roused, surely has intracranial bleeding.

Another important sign that develops in about half of the patients is a dilated pupil on one side—on the same side as the hemorrhage. The dilated pupil, when present, is of great value in localization, even more so than the motor paralysis. A large hematoma extending over almost an entire hemisphere has been found to produce a shift of the brain with resultant pressure on the brain stem of the contralateral side, giving rise to confusing motor symptoms. The dilated pupil in these instances is of more reliable localizing value than the motor paralysis.

Fourteen of the patients in this series had a dilated pupil, and in 13 of these, the hemorrhage was found on the side indicated by the pupil. In 4 of the patients, the paralysis was present on the same side as the dilated pupil, and in each instance the pupil was the deciding factor in the correct diagnosis, for the hematoma was located on that side.

If the extradural hemorrhage is not removed surgically, the pulse and respiration rates will remain low as long as the medullary centers can tolerate the pressure; but with failure of the medullary centers, the pulse and respiration rates and the temperature will continue gradually to rise until the patient dies. A rising pulse in a comatose patient is a danger sign of a failing medulla. Another important sign of excessive pressure on the medulla is the development of extensor spasms of the extremities known as decerebrate rigidity. In 5 of the patients with middle meningeal hemorrhage decerebrate rigidity developed prior to operation, and none of these recovered.

Case 1.—A white man aged 58 was struck by an automobile while crossing an intersection. He was accompanied by his wife.

After momentary unconsciousness, he arose and walked unassisted to the curb. He asked his wife what had happened to him since he did not recall being struck. This occurred about 6:30 p. m.

About 8:30 p. m., he complained of a rather severe headache, placed his hand over the left part of the forehead and the left temple and admitted severe pain

3. Dandy, W. E.: Diagnosis and Treatment of Injuries of the Head, J. A. M. A. **101**:772-775 (Sept. 2) 1933.

in that region. At 10:00 p. m., he was unable to talk. The family noted twitchings at this time about the right side of the face and the mouth, and shortly thereafter he became unconscious and had a severe generalized convulsion. He could not be awakened after the convulsion. At 11:00 p. m., the family physician arrived and was angry at being called to attend a patient who was virtually dead. He advised them to call the coroner's office. I saw the patient a half hour later, when he was brought to the Los Angeles General Hospital. His condition was critical.

Examination revealed the patient in deep coma, with a pulse rate of 46, a respiration rate of 16 and blood pressure of 180 systolic and 90 diastolic. There was present complete flaccid paralysis of the right side of the body. The respiration was of the characteristic blowing variety; the inspirations were slow and deep, and the expirations were short and forceful. There was a puffing out of the cheeks with each expiration. The Babinski sign was positive bilaterally. The left pupil was greatly dilated. No time was taken for making roentgenograms or spinal puncture.

A subtemporal craniotomy was done on the left side with the patient under local anesthesia induced with 2 per cent procaine hydrochloride. Black tarry blood extruded immediately through the first perforator opening. A large extradural hematoma was found and removed; it extended over the temporoparietal region. The torn middle meningeal artery was found and sealed by electrocoagulation. A fine linear fracture also was found, crossing the meningeal groove. There was no depression of bone. The patient became conscious the following morning and made a good recovery.

CHRONIC SUBDURAL HEMATOMA

The type of hemorrhage just discussed is arterial in origin and develops in four to twelve hours after the injury. There is another type of hemorrhage that is venous in origin and therefore much slower in development. This type develops subdurally and may take many weeks or even months to form; it is therefore known as chronic subdural hematoma.[4] Eighteen of the patients in this series had hemorrhage of this type.

This hemorrhage originates from a torn venous sinus or a large cortical vein, entering the longitudinal sinus. This interesting lesion consists of a collection of semiliquid blood in the subdural space and differs from the extradural type in that it becomes encapsulated and is never absorbed. The blood is eventually broken down and the pigment slowly removed until finally, in a hematoma of long duration, an encapsulated collection of clear fluid results. I have observed this

4. Kunkel, P. A., and Dandy, W. E.: Subdural Hematoma: Diagnosis and Treatment, Arch. Surg. **38**:24-54 (Jan.) 1939. Rand, C. W.: Chronic Subdural Hematoma, ibid. **14**:1136-1165 (June) 1927. Dandy.[1]

condition in 1 patient with a history of mental symptoms of many years' duration. The capsule in this instance was calcified to the extent that drill and rongeurs were necessary to open it.

These patients may occasionally go on for many years complaining of headaches; frequently mental symptoms develop. In these cases, brain tumor is suspected, even after ventriculographic studies. In 4 of these 25 cases, the diagnosis was made only after ventriculographic studies, and in 3 of these, the subdural blood was discovered through the burr hole made for the ventriculogram.

At operation, the presence of chronic subdural hematoma is a most welcome sight, since it is one of the most benign of the lesions which give rise to the increased intracranial pressure.

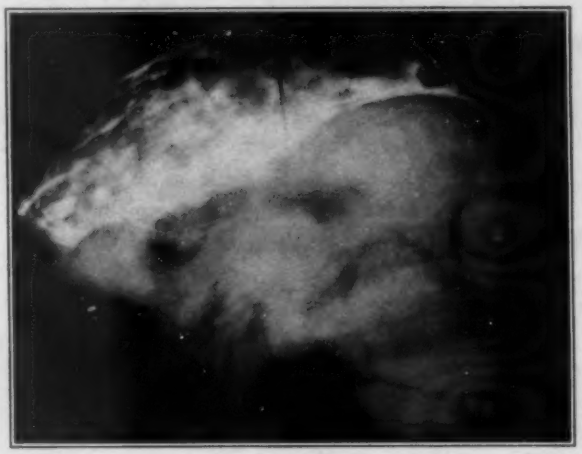

Fig. 2.—Roentgenogram of the brain, showing a calcified subdural hematoma. The patient had symptoms of forty years' duration.

CHRONIC SUBDURAL HYDROMA

Another interesting intracranial lesion is chronic subdural hydroma.[5] This consists of an encapsulated collection of clear fluid in the subdural space following an injury to the head. Cerebrospinal fluid passes into the subdural space through a tear in the arachnoid membrane; it becomes encapsulated and gives a clinical picture identical with that of chronic subdural hematoma. The correct diagnosis is made only at operation; recovery is usually complete.

CASE 2.—A laborer aged 70 fell over an iron pipe while at work and bruised his left shoulder. He was sent home and returned to work the following morning.

5. Coleman, C. C.: Chronic Subdural Hematoma, Am. J. Surg. **28**:341-363 (May) 1935. Naffziger, H. C.: Subdural Fluid Accumulations Following Head Injury, J. A. M. A. **82**:1751-1752 (May 31) 1924. Dandy.[1]

Although he did not feel well, he continued working with interrupted periods of illness for about five weeks.

Five and one-half weeks after the injury, he complained of headaches for the first time. Three days later, he began to limp with his right leg, and within the next two days, he became confused and drowsy and had urinary incontinence for the first time. A few hours later, he became comatose and exhibited a weakness of the entire right side of the body with a positive Babinski sign on the right.

The family physician made a diagnosis of cerebral thrombosis but, not being certain, called Dr. J. P. Fitzgibbon, who made the diagnosis of chronic subdural hematoma. I saw the patient on the same night at the Cedars of Lebanon Hospital. The patient was now in deep coma with complete flaccid paralysis of the entire right side. The pupils were small and equal. The temperature and the pulse and respiration rates as well as the spinal fluid findings were normal.

I operated on the patient the same evening. Massive chronic subdural hematoma was found on the left and chronic subdural hydroma on the right. The patient became conscious in six hours. Recovery was complete.

An acute brain injury is sometimes mistaken for an interval hemorrhage.[3] This type of patient is rendered immediately unconscious and remains so for an indefinite period—many hours or even days. In these patients, a rapid, bounding pulse, rapid moist breathing and a gradual rise in temperature develop early. There is often an associated injury to the midbrain or the pons in these acutely ill patients.

Persons with alcoholism who have received a concussion may, several hours after the injury, become comatose, and a low pulse rate may be present. They seem to fall into a deep sleep for many hours, and if they are permitted to lie flat on their backs, the relaxed tongue falls back and obstructs the breathing; this gives rise to stertorous sounds and at times even resembles the Cheyne-Stokes type. A patient of this type occasionally will have a generalized convulsive seizure. Careful observation, as well as the absence of focal or localizing signs, and history of alcoholic intoxication prior to the injury will aid in making the correct diagnosis.

Figure 2 is used with the permission of Dr. C. B. Courville.

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PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second Class Matter July 10, 1925, at the Postoffice at Chicago, Under the Act of Congress of March 3, 1879

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SHOCK PRODUCED BY CRUSH INJURY

EFFECTS OF THE ADMINISTRATION OF PLASMA AND THE LOCAL APPLICATION OF COLD

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AND

ALFRED BLALOCK, M.D.

BALTIMORE

In a previous paper [1] we described a method for producing experimental shock in which an attempt was made to simulate the crush syndrome in patients. The method consisted in placing a posterior extremity of the anesthetized animal in a mechanical press which had uneven surfaces. It was found that removal of the extremity from the press after five hours was followed by swelling of the thigh, an increase in the concentration of the blood, a decline in blood pressure, oliguria, abnormal urinary findings, elevated blood creatine and creatinuria and usually death. There was a large loss of plasma into and near the crushed area.

Only 1 of 19 animals in which the press was in place for five hours survived, despite the fact that all the animals appeared to be in good condition at the time the press was removed. On the other hand, it was found that 15 of 21 additional animals survived when a pneumatic tube exerting a pressure of 40 mm. of mercury was applied to the extremity immediately following the removal of the press. This was due presumably to a lessening of the local loss of fluid. There was no evidence that the pneumatic tube caused venous obstruction.

The present experiments were carried out in an attempt to prevent by other means the peripheral circulatory failure which follows this type of crush injury. The measures that were used in some experiments consisted in the intravenous administration of blood plasma equal in amount to the average loss into and near the injured area as reported in the

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1. Duncan, G. W., and Blalock, A.: The Uniform Production of Experimental Shock by Crush Injury: Possible Relationship to Clinical Crush Syndrome, Ann. Surg. **115**:684, 1942.

previous studies. In other experiments the effects of the local application of ice to the injured area were determined. In some instances the extremity was surrounded with ice during the entire five hour period that the press was in position. In the remaining experiments the extremity was cooled after removal of the press.

METHODS AND RESULTS

The method which was used in causing the crush injury was the same as that reported in the previous paper.[1] Several points should be emphasized. Medium-sized dogs, weighing between 7 and 11 Kg., were used in all experiments. Animals were chosen which had a good deal of muscular tissue in the thigh. The press was placed on the thigh in such a manner that the position of the femur corresponded to the groove in the triangular strips of wood. Pain was prevented by the use of anesthesia; the anesthetics were given in the doses which were used in the previous experiments.

Effects of Injecting Plasma.—The average difference in the weights of the crushed and noncrushed extremities in our first experiments amounted to 3.3 per cent of the body weight. As stated in our report, 20 of 21 animals in the control nontreated group died after removal of the press. The average survival time was slightly less than eight hours. In the present experiments, the intravenous administration of blood plasma from a second animal was begun immediately after the removal of the press. The plasma was administered slowly over a two hour period in most experiments, the shortest period being one hour. A total of 15 experiments was performed. The decline in blood pressure following removal of the press and during the time that the plasma was being administered was not so abrupt as that observed in the previously reported control experiments. It is to be noted, however, that in several experiments significant declines did occur during this period. An increase in the concentration of the blood was found in all the experiments, but again the alterations were not so great as previously noted in the untreated group. An increase in the pulse rate was found to occur in all experiments. The average elevation of rectal temperature was 2.3 F. These values are given in table 1.

Nine of the 15 animals died at intervals of thirteen to forty hours after removal of the press, the average survival time of this group being twenty hours. Alterations in nonprotein nitrogen, plasma creatine and plasma creatinine and urinary creatine and creatinine were greater in these 9 animals than were the changes in comparable periods in the 6 animals that survived. Similar differences were noted in the two groups on gross and microscopic examination of the urine. The urine of all the animals became grossly bloody within one hour after the press was removed. The urine of animals succumbing in forty hours or less showed numerous red cell casts and granular casts. Only 2 of the animals that survived showed granular or red cell casts, and these were few in number. The studies on the blood and the urine of 2 of the 9 animals that died are given in table 2.

As has been stated, the average difference in the weights of the injured and noninjured extremities in the control nontreated animals equaled 3.3 per cent of the body weight, and it is for this reason that it was decided in the present experiments to give plasma in quantities corresponding to this difference. Following the death of the 9 animals in the present group of experiments, the difference in the weights of the injured and noninjured posterior extremities

was determined by a bisection method.[2] This difference varied from 4.06 to 6.04 per cent, the average difference being 5.33 per cent. If one can assume that the experiments were identical except for the introduction of plasma into the animals of the present group, the figures show that only about two thirds of the plasma which was injected was lost at the site of injury. These figures are given in table 1.

It has been stated that 6 of the animals survived the immediate effects of the crush injury. This group includes 1 animal which died twenty-three days later. The cause of death of this animal was not determined with certainty, but the most significant observations included small amounts of free fluid in both pleural cavities, areas of focal necrosis in the liver and extensive scarring and fibrous replacement of a large part of the skeletal muscle of the thigh. The remaining 5 animals were observed for at least forty days. As stated previously, the changes observed in the blood and the urine were not so great in these 6 animals as in the animals which died within forty hours. The plasma creatine levels showed an average increase of 2 mg. per hundred cubic centimeters at the end of four to six hours and 2.6 mg. per hundred cubic centimeters at the end of twenty-four hours. The plasma creatinine levels had increased 0.3 mg. per hundred cubic centimeters at the end of four to six hours and 0.9 mg. per hundred cubic centimeters at the end of twenty-four hours. Both creatine and creatinine levels in the plasma had returned to normal at the end of forty-eight hours and remained within normal limits throughout the period of observation.

The nonprotein nitrogen levels of the blood of this group of animals showed an average increase of 11.4 mg. per hundred cubic centimeters at the end of four to six hours and at the end of twenty-four hours an average increase of 41.4 mg. per hundred cubic centimeters. Elevation of the nonprotein nitrogen was present in 3 of the 6 animals at the end of forty-eight hours, but all had reached normal levels by the fourth day. Subsequent frequent determinations showed occasional transient elevations of nonprotein nitrogen in all animals during the succeeding thirty-five to fifty days of observation.

The urinary output of these 6 animals at the end of four to six hours averaged 60 cc.; during the remainder of the first twenty-four hours, the average output was 48 cc. The gross hematuria which was present in all animals for the first twenty-four hours had cleared up at the end of forty-eight hours. The urinary output had increased to normal by the end of forty-eight hours and remained within normal limits throughout the period of observation. The urinary creatine and creatinine returned to the range of the control levels by the end of forty-eight hours, and no further elevations were observed.

Extensive injury to the compressed extremity resulted in all 15 experiments. Massive swelling, becoming maximal in six to eight hours, always followed removal of the press. In all experiments, the swelling of the injured extremity of the animals treated with plasma was greater than that of the control untreated animals. Examination of the thigh revealed extravasation of yellow fluid into the muscles, along fascial planes and into the subcutaneous tissues of the extremity and the adjacent body wall. The swelling was later complicated by the presence of either superficial or deep infection of the thigh so that the duration of the swelling due to plasma loss per se could not be accurately determined. Five of the 6 animals showed necrosis of the skin with superficial ulceration at the sites

2. Blalock, A.: Experimental Shock: A Cause of Low Blood Pressure Produced by Muscle Injury, Arch. Surg. **20**:959 (June) 1930.

TABLE 1.—*Showing the Effects of Introducing Blood Plasma After Having Caused Crush Injury*

Experiment Number	Mean Arterial Pressure, Mm. of Mercury		Hematocrit Reading		Pulse Rate per Minute		Respiratory Rate per Minute		Temperature, F.		Hours Press Was Applied	Therapy	Survival After Press Was Removed	Fluid Loss, per Cent of Body Weight	Examination of the Injured Extremity
	Control	Reading 6 to 8 Hr. After Press Was Removed	Control	Reading 6 to 8 Hr. After Press Was Removed	Control	Reading 6 to 8 Hr. After Press Was Removed	Control	Reading 6 to 8 Hr. After Press Was Removed	Control	Reading 6 to 8 Hr. After Press Was Removed					
1	110	40	35.2	44.3	120	200+	6	14	100.1	103.2	5	Plasma, 3.3% of body weight	Recovered	....	Marked swelling of the thigh, which persisted in the region of the knee joint; patellar reflex absent; posterior dislocation of the knee joint; necrosis of the skin at the site of the teeth of the press; deep infection in the thigh and suppurative arthritis of the knee joint developed
2	120	105	45.6	63.0	160	200+	10	10	99.4	100.8	5	Plasma, 3.3% of body weight	15 hr.	5.97	Marked swelling of the thigh consisting of yellow fluid in the muscles, along the fascial planes and the body wall
3	115	110	54.0	68.0	116	200	6	10	101.3	102.2	5	Plasma, 3.3% of body weight	29 hr., 45 min.	5.24	Marked swelling of the thigh consisting of yellow fluid in the muscles, along the fascial planes and the body wall
4	125	115	48.9	60.7	120	132	8	16	101.3	103.7	5	Plasma, 3.3% of body weight	20 hr., 15 min.	4.76	Marked swelling of the thigh consisting of yellow fluid in the muscles, along the fascial planes and the body wall
5	120	120	48.6	59.7	120	200	8	6	98.5	102.6	5	Plasma 3.3% of body weight	23 days	No swelling at time of death	Marked swelling of the thigh, which persisted approximately 20 days; footdrop present and patellar reflex absent—this persisted until death; ulceration of the skin persisted approximately 20 days; marked fibrosis of muscle of the thigh
6	125	90	40.5	55.4	116	200	12	36	101.6	103.0	5	Plasma, 3.3% of body weight	Recovered	....	Marked swelling of the thigh, which persisted approximately 21 days; necrosis of the skin with

														time of death	of the skin persisted approximately 20 days; marked fibrosis of muscle of the thigh
6	125	90	40.5	55.4	116	200	12	36	101.6	103.0	5	Plasma, 3.3% of body weight	Recovered	....	Marked swelling of the thigh, which persisted approximately 21 days; necrosis of the skin with ulceration which persisted approximately 19 days; footdrop persisted approximately 34 days; patellar reflex absent 28 days
7	125	125	41.4	49.4	124	172	6	8	100.7	103.2	5	Plasma, 3.3% of body weight	Recovered	....	Marked swelling which persisted 6 to 7 days; patellar reflex absent 31 days; footdrop persisted approximately 14 days; no skin necrosis
8	125	95	46.8	58.4	136	124	6	16	100.2	102.4	5	Plasma, 3.3% of body weight	13 hr.	6.04	Marked swelling of the thigh consisting of yellow fluid in the muscles, along the fascial planes and the body wall
9	140	105	54.8	71.3	116	200	10	10	100.7	100.8	5	Plasma, 3.3% of body weight	13 hr.	5.08	Marked swelling of the thigh consisting of yellow fluid in the muscles, along the fascial planes and the body wall
10	125	100	45.4	56.7	132	188	12	10	99.8	103.1	5	Plasma, 3.3% of body weight	Recovered	....	Marked swelling of the thigh; necrosis of a large area of skin with development of infection in this area; marked scarring in the skin and the subcutaneous tissue; absence of the patellar reflex persisted
11	130	90	49.2	78.4	120	200+	8	40	101.4	104.3	5	Plasma, 3.3% of body weight	14 hr.	5.81	Marked swelling of the thigh consisting of yellow fluid in the muscles, along the fascial planes and the adjacent body wall
12	125	85	48.5	62.4	112	200+	8	14	99.7	102.2	5	Plasma, 3.3% of body weight	Recovered	....	Marked swelling of the thigh which persisted approximately 11 or 12 days; necrosis of the skin at the site of the press teeth persisted approximately 17 days; footdrop persisted 34 days; patellar reflex remained absent until death by killing on the fortieth day
13	125	120	45.4	69.0	100	180	6	16	98.8	102.6	5	Plasma, 3.3% of body weight	14 hr.	5.35	Marked swelling of the thigh consisting of yellow fluid in the muscles, along the fascial planes and the adjacent body wall
14	120	100	49.7	58.6	136	200+	6	16	101.4	103.6	5	Plasma, 3.3% of body weight	40 hr.	4.06	Marked swelling of the thigh consisting of yellow fluid in the muscles, along the fascial planes and the adjacent body wall; swelling was less marked at the time of death
15	130	80	53.7	62.3	136	200+	8	8	99.8	103.2	5	Plasma, 3.3% of body weight	13 hr.	5.05	Marked swelling of the thigh consisting of yellow fluid in the muscles, along the fascial planes and the adjacent body wall

where the greatest pressure had been exerted by the wooden teeth of the press. Two of the group had more extensive deep-seated infections of the thigh, and these infections resulted in extensive scarring. Footdrop which persisted for periods varying from fourteen to thirty-four days developed in 4 animals. The presence or absence of footdrop in the 2 animals with deep infections could not be ascertained because of failure to use the extremity in walking. The patellar reflex was absent in all animals—for twenty-eight and thirty-one days in 2 animals and until death or killing in the other 4. One animal sustained a posterior dis-

TABLE 2.—*Urinary and Blood Findings as Affected by Crush Injury and Plasma Therapy*

Experiment Number	Test	Control Reading	Reading After Press Was Removed		Comment
			4-6 Hr.	24 Hr.	
3	Nonprotein nitrogen, mg. per 100 cc.	34.2	....	98.9	Urine became grossly bloody within one hour after press was removed; microscopic examination of the urine following removal of the press showed numerous granular and red cell casts and numerous erythrocytes; the total output of urine following removal of the press was 78 cc.; died after 29 hours, 15 minutes
	Plasma creatine, mg. per 100 cc.	0.9	....	12.9	
	Plasma creatinine, mg. per 100 cc.	2.1	....	6.6	
	Hematocrit	54.0	64.2	70.0	
	Urine output, cc.	....	40.0	38.0	
	Gross examination	Clear yellow	Bloody	Bloody	
	Urine creatine, mg. per 100 cc.	0.5	....	2.8	
	Urine creatinine, mg. per 100 cc.	2.8	....	1.5	
14	Nonprotein nitrogen, mg. per 100 cc.	21.5	36.0	129.0	Urine became grossly bloody within 1 hour after the press was removed; microscopic examination of the urine following removal of the press showed numerous granular and red cell casts and numerous erythrocytes; the total output of urine from the time of removal of the press until death at 40 hours was only 110 cc.
	Plasma creatine, mg. per 100 cc.	1.4	10.2	13.5	
	Plasma creatinine, mg. per 100 cc.	1.1	2.3	4.0	
	Hematocrit	49.7	54.0	....	
	Urine output, cc.	....	15.0	23.0	
	Gross examination	Clear yellow	Bloody	Bloody	
	Urine creatine, mg. per 100 cc.	0.9	4.5	3.1	
	Urine creatinine, mg. per 100 cc.	0.9	0.6	0.6	

location of the knee joint of the crushed extremity, and subsequent development of suppurative arthritis of this joint was observed. Section of the injured thigh of a number of animals revealed extensive scarring and fibrous replacement of a large part of the skeletal muscle.

EFFECTS OF THE LOCAL APPLICATION OF COLD

Nineteen experiments with the local application of cold were performed. The results are summarized in table 3.

Simultaneous Application of Mechanical Press and of Ice.—In 7 experiments, the extremity was surrounded with ice immediately after application of the press, and this arrangement was maintained during the five hour compression period. Two animals succumbed, the one surviving thirteen hours and the other five

days. At autopsy the lungs of both animals showed findings suggestive of pneumonia. In the animal which died in thirteen hours there was fluid loss into the injured extremity of only 0.59 per cent of the body weight.

Alterations of the criteria under observation in this group were minimal when compared with those observed in the untreated animals previously reported. In 3 of the 7 experiments, arterial pressure declined to 100 mm. of mercury or slightly below; the average fall for the group was 10.7 mm. of mercury. Hemoconcentration was observed in all experiments but was not marked. The average increase in the pulse rate was 34.6 per minute. The respirations increased in 1 animal, decreased in 4 and remained unchanged in 2. The oral temperature declined in all animals while the ice was on the thigh but returned to approximately the normal level by the end of six to eight hours. In all experiments rectal temperatures were lowered to a greater degree than the oral temperatures because of the proximity of the ice to the rectum.

The 5 surviving animals were observed for at least twenty-three days. Examination of the injured extremity revealed only slight swelling after removal of the press. The injury to the skin and the muscles was not so great as in the untreated animals referred to previously. No severe infections of the injured extremity occurred. In these animals, the urinary output was greater following the removal of the press than it was in the untreated animals or in those animals which survived after treatment with plasma. Gross blood was present in the urine of 2 animals; the urine of all the animals showed erythrocytes on microscopic examination, but in none of the group were casts observed at any time. In 4 animals in which blood nonprotein nitrogen, plasma creatine and creatinine and urinary creatine and creatinine were determined, the changes observed were only slightly above normal values. Subsequent determination of the nonprotein nitrogen showed occasional transient elevations which were unassociated with other evidence of kidney dysfunction.

Although the 7 experiments enumerated are of interest from an academic viewpoint in showing the protective influence of the local application of cold, it is obvious that one cannot thus chill an extremity of the patient who is pinned beneath debris. In order to attempt to approach more closely the conditions which are encountered in the care of patients, other experiments were performed in which the extremity was surrounded with ice thirty minutes after the removal of the press. During this interval a tourniquet was applied to the extremity in order to lessen the early local swelling that follows removal of the press.

Application of Cold Following Removal of the Press.—Twelve experiments of this type were performed. In 6 of the experiments, the crushing apparatus was left on the thigh for five hours. On removal at the end of this time, a tourniquet was applied to the upper part of the thigh. Thirty minutes after the press was removed and the tourniquet applied, the extremity was packed in ice. One hour later the tourniquet was removed, the ice being left on the thigh for the ensuing four hours. The remaining 5 experiments were performed in an identical manner except that the crushing apparatus was applied for three and one-half hours instead of five hours.

In the experiments in which the extremity was compressed for five hours before the application of ice, all animals died; the average duration of life was eleven and five-tenths hours. The average fluid loss into the injured extremity was 3.7 per cent of body weight. Three of 5 animals to which the crushing apparatus was applied for three and one-half hours died in an average time of eighteen and three-tenths hours. The average fluid loss into the injured extremity

TABLE 3.—*Effects of the Local Application of Cold Coincident with and Following Crush Injury*

Method of Therapy	Experiment Number	Mean Arterial Pressure, Mm. of Mercury		Hematocrit Reading		Pulse Rate per Minute		Respiratory Rate per Minute		Temperature, F.		Hours Press Was Applied	Survival After Press Was Removed	Fluid Loss, per Cent of Body Weight	Examination of the Injured Extremity
		Control	Reading 4 to 7 Hr. After Press Was Removed	Control	Reading 4 to 7 Hr. After Press Was Removed	Control	Reading 4 to 7 Hr. After Press Was Removed	Control	Reading 4 to 7 Hr. After Press Was Removed	Control	Reading 4 to 7 Hr. After Press Was Removed				
Extremity packed in ice during the entire period of compression	1	125	100	49.9	55.4	140	168	10	6	101.8	97.7	5	Recovered	....	Slight swelling of the extremity after removal of the press; no skin necrosis; footdrop persisted 34 days; patellar reflex absent 20 days
	2	120	95	51.0	52.2	124	172	8	10	98.6	101.0	5	Recovered	....	Slight swelling of the thigh following removal of the press; no skin necrosis or ulceration; patellar reflex normal; footdrop persisted 31 days
	3	130	130	53.8	59.4	124	196	10	6	99.2	99.8	5	Recovered	....	Slight swelling of the extremity following removal of the press; no skin necrosis or ulceration; no loss of the patellar reflex; footdrop persisted 24 days
	4	120	120	45.6	59.7	140	178	10	8	100.3	99.8	5	Died, 13 hr.	0.59	Slight swelling of the thigh; pneumonia in both lungs; more marked involvement of the right lung
	5	115	115	50.4	52.6	148	172	12	8	101.0	98.8	5	Recovered	....	Slight swelling of the thigh; no skin ulceration; no loss of patellar reflex; footdrop persisted 28 days
	6	115	105	43.8	44.3	152	160	12	12	99.0	101.2	5	Recovered	....	Slight swelling of the thigh; no skin ulceration; footdrop persisted and patellar reflex was absent at the end of 23 days
	7	115	100	49.7	57.6	96	120	6	6	99.0	98.4	5	Died, 5 days	....	Swelling of the thigh slight and not demonstrable at the end of 24 hours; bloody nasal discharge 2 days before death; patchy pneumonia in the right lung; hemorrhage into the colon and the lower part of the ileum
Tourniquet applied	8	120	100	43.6	61.4	116	200+	8	12	100.2	94.0	5	Died, 12 hr.	3.75	Moderate swelling of the thigh; yellow fluid in the

														at the end of 24 hours; bloody nasal discharge 9 days before death; patchy pneumonia in the right lung; hemorrhage into the colon and the lower part of the ileum
Tourniquet applied to the thigh as the press was removed; 30 min. later the thigh was packed in ice; 30 min. later the tourniquet was removed; the thigh was left in ice 4 hr.	8	120	100	43.6	61.4	116	200+	8	12	100.2	94.0	5	Died, 12 hr.	3.75	Moderate swelling of the thigh; yellow fluid in the muscles, along the fascial planes and the adjacent body wall
	9	130	100	61.3	81.0	128	158	6	16	98.7	98.6	5	Died, 11 hr.	4.05	Moderate swelling of the thigh; yellow fluid in the muscles, along the fascial planes and the adjacent body wall
	15	115	110	48.8	70.5	96	130	10	8	99.4	97.4	5	Died, 12 hr.	4.68	Moderate swelling of the thigh; yellow fluid in the muscles, along the fascial planes and the adjacent body wall
	16	115	115	56.0	69.2	108	186	8	10	99.0	97.0	5	Died, 13 hr.	3.12	Moderate swelling of the thigh; yellow fluid in the muscles, along the fascial planes and the adjacent body wall
	17	115	70	49.2	71.2	104	180	8	10	99.8	90.0	5	Died, 11 hr.	2.73	Moderate swelling of the thigh; yellow fluid in the muscles, along the fascial planes and the adjacent body wall
	18	120	100	53.3	80.4	140	200+	10	6	100.4	92.4	5	Died, 10 hr.	3.24	Moderate swelling of the thigh; yellow fluid in the muscles, along the fascial planes and the adjacent body wall
Tourniquet applied to the thigh as the press was removed; 30 min. later, the thigh was packed in ice; 30 min. later, the tourniquet was removed; the thigh was left in ice 4 hr.	10	100	85	35.2	51.4	112	200	16	8	102.2	100.2	3½	Recovered	....	Marked swelling of the thigh; later severe deep infection developed in the thigh; patellar reflex was absent and footdrop persisted at 16 days
	11	125	115	47.7	68.3	120	132	8	6	100.6	87.0	3½	Died, 5 hr.	3.44	Marked swelling of the thigh; yellow fluid in the tissues of the thigh and on the adjacent body wall
	13	115	70	43.0	55.0	112	200+	8	20	101.0	99.0	3½	Recovered	....	Marked swelling of the thigh; deep infection of the thigh and sloughing of the toes and the lateral surface of the thigh developed; footdrop and absent patellar reflex persisted at 9 days
	14	120	105	51.4	75.2	124	200+	12	4	99.0	94.0	3½	Died, 40 hr.	2.50	Marked swelling of thigh had diminished some at the time of death; yellow fluid in the tissues of the thigh and the adjacent body wall
	15	125	75	56.0	70.2	120	200+	10	10	101.3	93.6	3½	Died, 10 hr.	3.09	Marked swelling of the thigh; yellow fluid in the tissues of the thigh and on the adjacent body wall

was 3.0 per cent of body weight. A decline in arterial pressure was observed in both groups at the end of six to eight hours but was not so great as the decline observed in the untreated control animals. Marked hemoconcentration was observed in all experiments. An increase in the pulse rate occurred in all experiments, the average being approximately the same in the two groups. The body temperature declined in all animals; the average fall in temperature for the two groups was 5.3 F. When observed at corresponding periods after removal of the press, the 2 animals which survived did not show so great a fall in body temperature as did the others.

In all experiments the output of urine was decreased. Grossly bloody urine was observed in all experiments in which the extremity was crushed for five hours. Red cell casts and granular casts were noted in 4 of the 6 experiments. In the experiments in which the extremity was compressed for three and a half hours, gross blood was present in the urine of 3 animals, and granular and red cell casts were observed in only 2.

Swelling of the injured extremity was pronounced in all experiments. In the 2 surviving animals, severe infections of the thigh developed, resulting in extensive scarring. Footdrop and absent patellar reflex were noted in one animal at the end of nine days and in the other at the end of sixteen days.

COMMENT

In our previous publication [1] on this subject, attention was focused on the method and on the early effects of the injury. It was stated that practically all the animals subjected to this form of injury die, the average survival time being seven and fifty-five hundredth hours. One of the chief objects of the present experiments was to prolong life for a sufficient length of time in order to observe the animals during the later period which corresponds to that in which oliguria and uremia followed by death have developed in some of the reported clinical cases of crush syndrome. In 6 animals, the injection of plasma prolonged life sufficiently for observation of any similar changes. In these animals a large mass of muscle was crushed, and at least part if not all of the blood supply to an extremity was shut off for five hours. Swelling of the extremity, shock, oliguria, hematuria and the presence of casts in the urine developed after removal of the press, and these alterations simulated fairly closely the essential early features of the reported cases in human beings. In spite of the similarity of these features, the late development of oliguria and casts in the urine and uremia followed by death after several days with the characteristic pathologic findings in the kidneys has not been observed in these experiments. The urinary output of the animals under prolonged observation varied considerably but remained within normal limits. Occasional transient rises in nonprotein nitrogen occurred but were unassociated with oliguria and the presence of casts.

The fluid loss into the injured extremity of the dogs treated with plasma is of special interest when it is recalled that in the untreated control group the local fluid loss into the injured extremity was 3.3

per cent of body weight, whereas in the plasma-treated group the loss was 5.3 per cent of body weight. This observation indicates an additional fluid loss of 2 per cent of body weight into the injured area or almost two thirds of the plasma which was injected. Death resulted in 9 of the 15 animals in spite of the early injection of an amount of plasma equivalent to the average fluid loss which produced death in the untreated animals. Only two thirds of the injected plasma was accounted for, and that was lost locally at the site of injury. It seems likely that the absorption of toxic products played a part in causing the death of these animals.

Trauma to extremities followed by large intravenous infusions of solution of sodium chloride was shown by Harkins and McClure [3] to result in a local fluid loss into the extremity of 6.3 per cent of body weight as compared to an average local loss in traumatized untreated animals of 4.2 per cent of body weight. A local fluid loss of 5.6 per cent occurred in traumatized animals which were given large transfusions of whole blood. In our experiments the fluid lost into the traumatized area was almost entirely plasma. This plasma loss was due to local mechanical injury to the tissues plus the effects of five hours of partial or complete anoxia. The maintenance of the circulating blood volume and of the effective arterial pressure by the injection of plasma was probably responsible for the additional fluid loss into the injured area where gross injury to blood vessels and increased capillary permeability were present. In this connection it is of interest that in other experiments chilling of the part was effective in reducing the local loss of fluid.

The damage produced in the muscles of the thigh could be seen at the time of removal of the press. The muscle bundles were stretched and torn, and in some animals, entire muscles were severed. Late evidence of muscle damage was demonstrated by the extensive fibrosis of all the injured muscles. Necrosis of the skin occurred in most of the animals. In several animals, these areas of skin necrosis served as a portal of entry for organisms producing deep infections of the thigh.

The maintenance of the extremity at a low temperature during the time that the mechanical press was in place exerted a definitely protective influence. This protective influence was probably due to the fact that the metabolism of the tissues was reduced and that less injury resulted from the inadequate blood supply. On the other hand, cooling of the part following the removal of the press did little if any good. Under the latter condition the mechanical injury and the anoxia had already exerted their deleterious effects, and the subsequent lowering of the temperature did not lessen the local loss of fluid or the degree of the other alterations.

3. Harkins, H. N., and McClure, R. D.: The Present Status of Intravenous Fluid Treatment of Traumatic and Surgical Shock, Ann. Surg. **114**:891, 1941.

In several recent additional experiments, the press was left on the extremity for fifteen rather than for five hours. After removal of the press, blood plasma was administered intravenously in an amount slightly in excess of the local loss at the site of injury. These animals succumbed within twenty-four hours after removal of the press. The most likely cause of death in these animals appears to have been the absorption of toxic products from the extremity which had been subjected to gross trauma and prolonged ischemia. The duration of anesthesia is probably an additional factor. Further studies are indicated.

SUMMARY

Further studies on experimental crush injuries of extremities are described. Attempts were made to prolong the life of the animals by the injection of plasma equal in amount to the average local fluid loss into the extremities of untreated animals. In spite of this therapy, 9 of 15 animals died with an additional local fluid loss of approximately 2 per cent of the body weight into and about the injured area. The prolonged observations on the surviving animals are described.

The effects of the local application of ice to the injured extremity were studied. In some experiments, the extremity was refrigerated during the entire period of compression, whereas in others the ice was applied after the press had been removed. It was found that cooling of the extremity resulted in less local swelling and an increase in the survival rate if it was maintained during the entire compression period. Lowering of the temperature of the part after the damage had been caused did not appear to exert a favorable influence.

The results indicate that local fluid loss plus the absorption of toxic products was responsible for the death of these animals in which crush injury was produced. When the compression was maintained for several hours only, it was our impression that the local loss of plasma was the major factor in precipitating peripheral circulatory failure. When the compression of the extremity was maintained for many hours and when early death following release of the press was prevented by the administration of plasma, it is likely that the ultimate fatal outcome was due in the main to the effects from the absorption of toxic products.

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OSSEOSONOMETRY

I. THE USE OF PERCUSSION-AUSCULTATION IN FRACTURES

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Percussion over one end of a bone will set up audible vibrations that are clearly heard with a stethoscope at the other end. These vibrations are even transmitted through one or more joints and may be carried to distant points on the skeleton. It is usually forgotten in physical diagnosis that bone, the hard tissue, carries audible vibrations farther and more clearly than any solid organ or soft tissue. A simple experiment of listening with a stethoscope over the pubis, while a medial malleolus is struck with the finger, shows the distance a percussion note will be carried through bone and likewise illustrates the normal, distinct, low-pitched resonant note which is heard from bone percussion. This sound has a definite "osteal," almost metallic, quality. Other types of vibrations, such as those set up by a tuning fork or vibrator, also can be heard distinctly.

That other tissues and organs transmit and modify sound waves is well known. The principle of percussion established by Auenbrugger in 1755 and the principle of auscultation introduced by Laennec in 1818 have both proved to be extremely important clinical aids. Since the time of these authors, elaborate and reliable relations have been established between the alterations in sound phenomena and the pathologic changes in tissues and organs. It seems amazing that the same principles have not been widely applied to the clinical study and diagnosis of bone lesions.

This study deals only with fractures in long bones, although interesting changes in the percussion note have been found in other less common lesions. The aim has been to make this report of clinical value in the diagnosis and the treatment of fractures. There has been no thought of replacing the indispensable and extensive use of roentgen rays in fracture work. However, there are numerous occasions when

Aided by a grant from the Committee on Scientific Research of the American Medical Association.

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auscultation and percussion are available, when the fluoroscope is not and when even a hospital with x-ray apparatus is miles and minutes distant. The justification for the expense of an ambulance, a roentgen examination and hospitalization for an elderly lady who has tripped on a rug and injured her hip is usually obtained with the percussing finger and a stethoscope.

Case 1.—M. H., a woman aged 62 years, sustained an intracapsular fracture of the left hip (fig. 1). The diagnosis was made by percussion-auscultation before roentgenograms were taken because of a marked change in the quality of the note and a moderate diminution of the intensity observed in comparing the findings on the two legs. Percussion-auscultation from the patella to the symphysis was carried out on each side. After reduction and impaction and immobilization with a Smith-Petersen nail, the percussion note was almost indistinguishable on the two sides. This case illustrates figure 2.

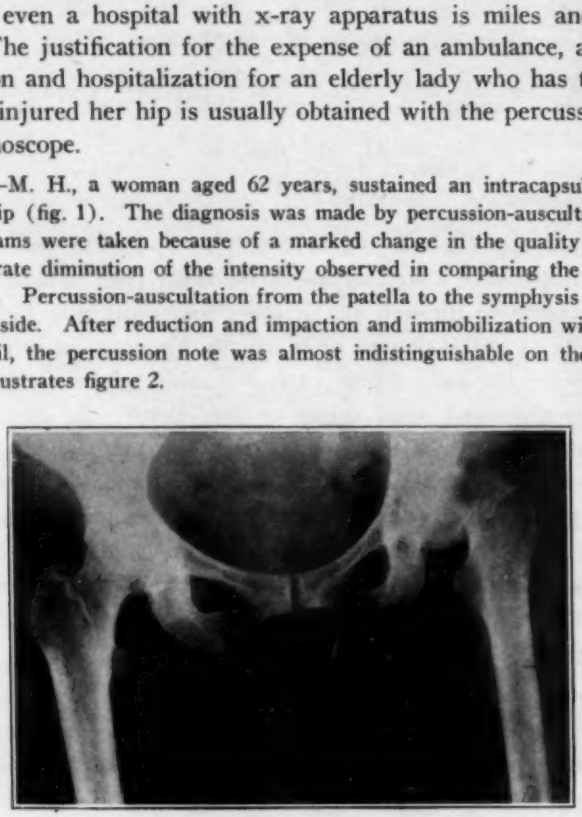


Fig. 1 (case 1).—Roentgenogram of an intracapsular fracture of the left hip. The diagnosis was made by percussion-auscultation before roentgen examination was made.

Information of great value about an injured extremity can thus be obtained with a minimum of delay and expense. That the examination can be carried out painlessly is appreciated by a patient. The injured extremity need not be moved, although it is necessary to place the uninjured one in a symmetric position for the comparative percussion-auscultation.

Fractures of the extremities lend themselves well to percussion-auscultation because there is almost invariably a normal intact bone available for comparison, and symmetric bony prominences are fairly numerous.

The properties of sound are intensity, quality and pitch. A solid elastic body, such as bone, can be set in vibration by percussion; it will

then tend to vibrate at its fundamental frequency or pitch. This frequency follows acoustic laws and depends on the size, the shape, the weight and the elasticity of each bone. The pitch is governed by the law of similar systems as stated by Kimball:[1] "When two vibrating systems are made of the same material, . . . their periods of vibration are proportional to their linear dimensions." As an example he stated that if one takes two steel bars, one of which has half the dimensions of the other, the smaller will make twice as many vibrations per second as the larger when vibrating in the same manner. The intensity of the sound wave will be affected by the laws of reflection, for in the transmission of sound waves from one medium (bone) to another (hematoma and soft tissue), most of the energy (intensity) goes into the reflected wave.[2] The quality of the wave will be modified in a frac-

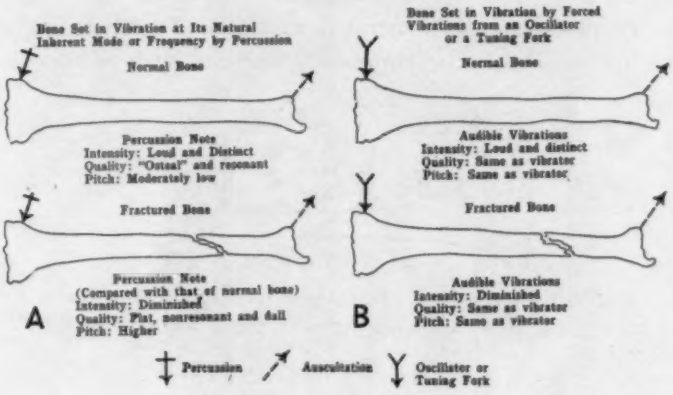


Fig. 2.—Types of vibrations.

ture both by the superficial characteristics of changed pitch and intensity and also by the overtones of the smaller fragments. Thus the ringing resonant quality is usually lost. Although percussion tends to set up a free vibration in bone, it is modified considerably by the dampening effect of soft tissue and muscle in which it is embedded in vivo. These primary findings, as illustrated in figure 2 *A*, show the effect of a simple fracture on the intensity, the quality and the pitch of the transmitted percussion note when compared to the note of the normal intact bone.

Solids or bones can be set into vibration also by a tuning fork or a vibrator (fig. 2 *B*). The bone will then be forced to vibrate at the same

1. Kimball, A. L.: College Text-Book of Physics, ed. 2, New York, Henry Holt & Company, 1917, p. 224.

2. Kimball,[1] p. 194.

pitch as the tuning fork. The note heard in the fractured bone will be the same as that heard in the intact bone except that the intensity will be changed. This use of the tuning fork was first described by Andrews [3] in 1903. This was the earliest paper found in a search of the literature on the acoustic phenomena of fractures. In 1929, Polera and Tripodi [4] also elaborated on the use of the tuning fork. They had excellent diagrams, and they described complex variations in the quality of the sound in various fractures. I have been unable to distinguish these variations in quality (fig. 2 *B*) and have found a modification of intensity only. The superiority of the use of percussion over the use of the tuning fork for clinical use will soon become apparent, because all three properties may be changed by a fracture.

The change in the intensity of the percussion note as produced by a fracture was first described by Vigevani [5] in 1925. His method of auscultatory percussion is illustrated in figure 3 and is particularly applicable to bones near the surface of the skin, such as the tibia and

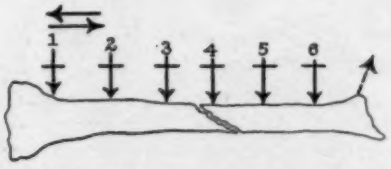


Fig. 3.—Vigevani's method of auscultatory percussion. Percussion is shifted either toward or away from the stethoscope. There is a change in the percussion note between 3 and 4.

the ulna. The stethoscope is held at one end of the bone, and the percussing point is shifted along the bone either toward or away from the listening end. Vigevani described a change in the intensity of the note as the fracture line is crossed by the percussing finger.

Case 2.—J. L., a man aged 22 years, had a compound comminuted fracture of the right tibia and fibula. There was extensive loss of skin on the medial surface (10 by 3 cm.); this wound healed in four months after skin grafting. A Steinmann pin was inserted in the os calcis and then incorporated in plaster. On July 16, 1937 (fig. 4 *A*), a marked change of percussion note was found at the fracture site by the method of Vigevani (fig. 3). On ordinary percussion-auscultation, the intensity was diminished, and the quality was dull and nonresonant when compared to the intact left tibia (fig. 5 *B*). Roentgenograms taken on Jan. 15, 1938, showed

3. Andrews, A. H.: The Tuning Fork and Stethoscope in the Diagnosis of Fractures, Chicago M. Recorder **24**:182-184 (March) 1903.

4. Polera, N., and Tripodi, A.: Diagnosis of Fractures by Phonometry, Rinasc. med. **6**:531-533 (Nov.. 15) 1929.

5. Vigevani, E.: Auscultatory Percussion in Fractures, Policlinico (sez. prat.) **32**:1783-1820 (Dec. 21) 1925.

slight endosteal callus (fig. 4 *B*). There was only slight change in the percussion note. The intensity was only slightly diminished, and the quality was almost normal and resonant (fig. 6 *A*). On May 18, 1940, roentgenograms showed solid healing with a large callus (fig. 4 *C*). The percussion-auscultation intensity was definitely increased over that found in the left tibia (fig. 6 *C*). The roentgenogram was taken because of cellulitis in the leg due to tinea infection in the right foot.

The change in the percussion note of a fractured bone is found to vary markedly according to the type of fracture and the position of the

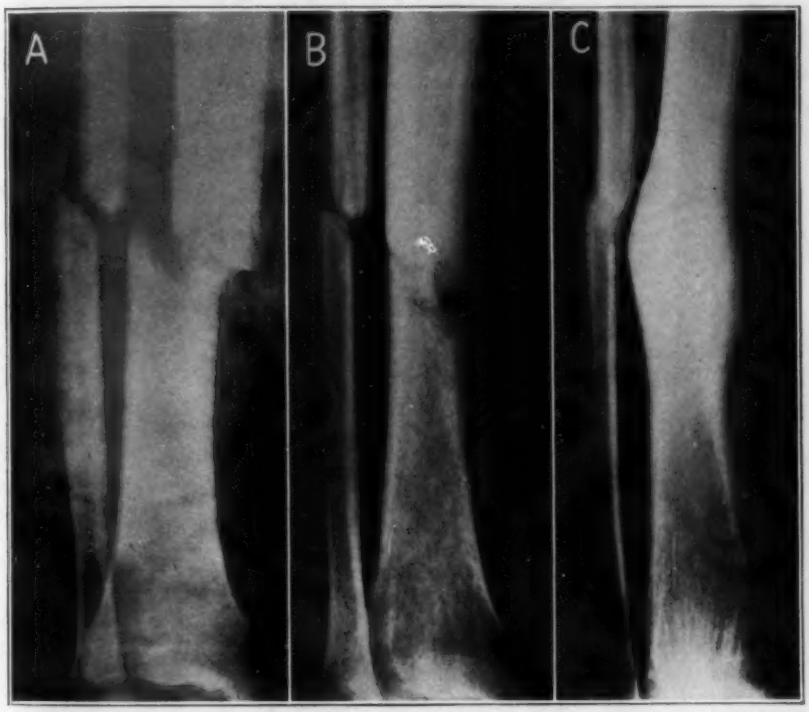


Fig. 4 (case 2).—The patient had compound comminuted fracture of the right tibia and fibula. *A*, roentgenogram taken on July 16, 1937. *B*, roentgenogram taken on Jan. 15, 1938, showing slight endosteal callus. *C*, roentgenogram taken on May 18, 1940, showing solid healing with a large callus.

fragments when percussion-auscultation is carried out. Some of these changes are illustrated in figure 5. The most dramatic change is found in a severely comminuted fracture or in one with overriding fragments (fig. 5 *A*). In fact, if the two major fragments are not in bony contact, no sound at all may be transmitted across the fracture (see initial reading in case 3); this also occurs if there is soft tissue interposition.

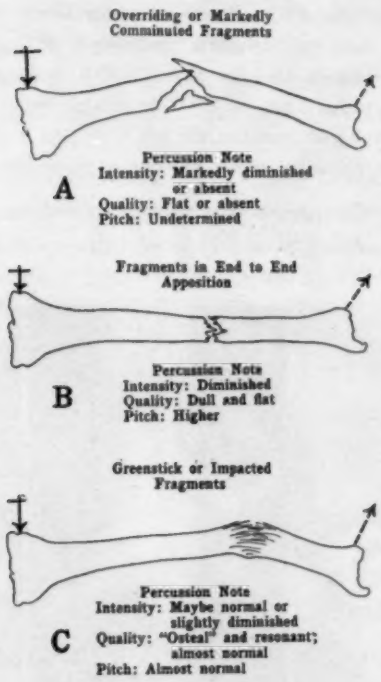


Fig. 5.—Effect of the position of fragments on the percussion note.

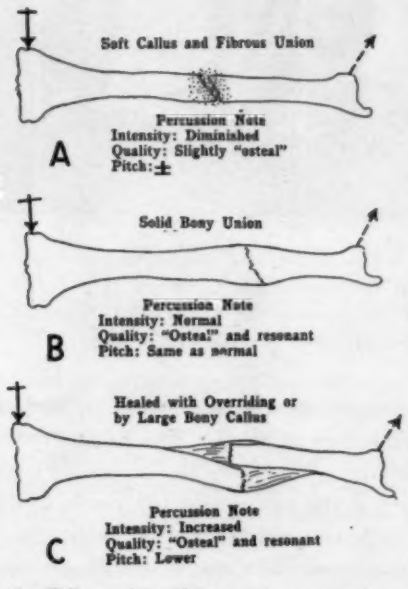
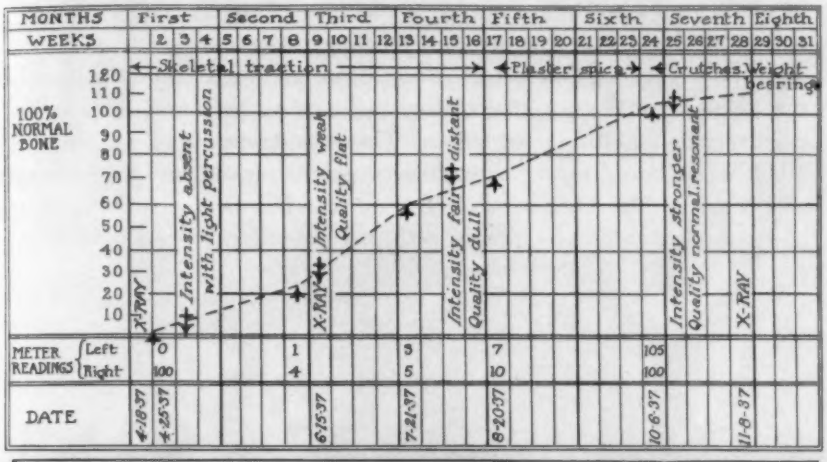


Fig. 6.—Effect of healing on the percussion note.

CASE 3.—I. M., a man, had a compound comminuted fracture of the femur. On admission, a light percussion stroke was not audible on auscultation, and the meter reading was 0. This illustrates the marked effect of a comminuted fracture, as shown in figure 5 *A*. On the next phonometric examination, eight weeks later, the meter reading was ¼, and the percussion note was now audible owing to the



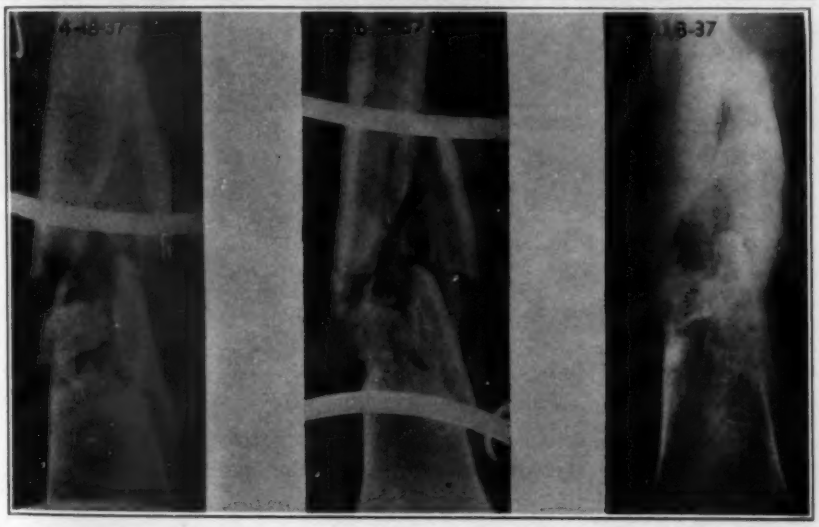


Fig. 7 (case 3).—The patient had a compound comminuted fracture of the femur. On admission, a light percussion stroke was not audible on auscultation, and the meter reading was 0. Eight weeks later the meter reading was ¼. Later readings disclosed a progressive increase in the intensity of the note to $^{9}/_{10}$ and then $^{72}/_{100}$. After immobilization, the meter readings were all over 100 per cent.

formation of slight intramedullary callus (fig. 6 *A*). Later readings disclosed a progressive increase in the intensity of the note to $^{9}/_{10}$, then $^{72}/_{100}$, as indicated on the chart in figure 7. Percussion-auscultation showed likewise a gradually increased

intensity of the note. After immobilization in a spica cast, the meter readings were all over 100 per cent, and the note heard on percussion-auscultation of the fractured femur was louder than that heard on percussion-auscultation of the control femur (fig. 6 *C*). Clinically, the bone was solid, and motion was begun.

This case illustrates how well the percussion-auscultation findings, the meter readings and the roentgen evidence all coincide in the diagnosis and progress of this fracture until healing was obtained.

If an overriding fracture is reduced into good end to end apposition, the intensity of the percussion note is found to be markedly improved over what it was before reduction. This was described by Lippman [6] in 1932, when he advocated auscultatory percussion during the reduction of a fracture. In other words, the better the fragments are reduced, the more nearly normal and intense will be the percussion note.

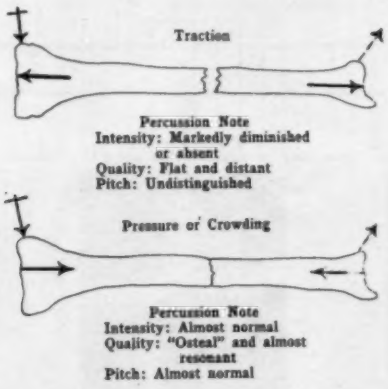


Fig. 8.—Effect of traction or pressure through joints or fragments.

Two types of fractures are extremely difficult of diagnosis by percussion-auscultation. Figure 5 *C* illustrates these two types. If a fracture is solidly impacted, the whole bone will vibrate as a unit and on auscultation will sound similar to the normal bone. Many greenstick or incomplete fractures fail to give acoustic evidence of fracture for the same reason. Likewise internal fixation, as in the nailing of intracapsular hip fracture, or plating or grafting of fractures, if solidly done, immediately changes the percussion notes so that they sound almost normal. This occurred in case 1 after immobilization with a Smith-Petersen nail.

The effect of traction on a fracture or on a joint during percussion-auscultation is illustrated in figure 8. Traction separating the fragments may completely abolish all transmission of sound. These factors are of

6. Lippman, R. K.: The Use of Auscultatory Percussion for the Examination of Fractures, J. Bone & Joint Surg. **14**:118-126 (Jan.) 1932.

great clinical value during traction. In making the diagnosis of a fracture, if the signs are not clearcut, traction on both extremities will accentuate or clarify the findings.

CASE 4.—T. L., a man aged 56, had a compound fracture of the lower third of the right femur with a small uninfected puncture wound. A large hematoma developed and was aspirated twice. Skeletal traction of 30 pounds (13.6 Kg.) was applied through the tibial tubercle. On admission, the intensity by percussion-auscultation was markedly diminished and the quality dull (fig. 9 *A*). One week later (fig. 9 *B*) on percussion-auscultation, the note was absent entirely. Diagnosis of overpull and separation of fragments was made by percussion-auscultation before roentgenograms were taken because no sound at all was transmitted through the

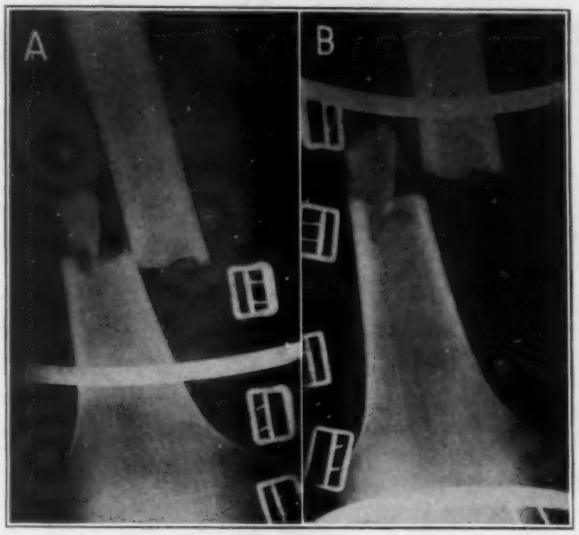


Fig. 9 (case 4).—*A*, roentgenogram taken on March 1, 1941, on admission, showing a compound fracture of the lower third of the right femur. *B*, roentgenogram taken one week later.

femur. Traction was reduced to 15 pounds (6.8 Kg.). The fracture healed with slight overriding.

During this study it soon became apparent that the percussion note in an individual fracture slowly changed as healing and callus formation progressed. These changes are shown in figure 6. As the callus gets stiffer and stronger (fig. 6 *A* and *B*), the percussion note more and more approaches that of the normal bone. It may even, as in figure 6 *C*, surpass the normal bone in intensity if the fracture heals with excessive callus, which may act as a flywheel or pendulum during the vibrations. These changes are illustrated by cases 2 and 3.

This change has been of value in determining the healing of fractures in certain cases. For example, in intracapsular fractures which have not been nailed, the roentgen evidence of healing is not always convincing because little periosteal callus is visible. Percussion-auscultation in these cases may furnish valuable evidence of the degree of healing.

The method in general is shown in figure 10. This illustrates the most convenient bony points for the percussion and auscultation of various bones. It is always advisable to place the uninjured extremity

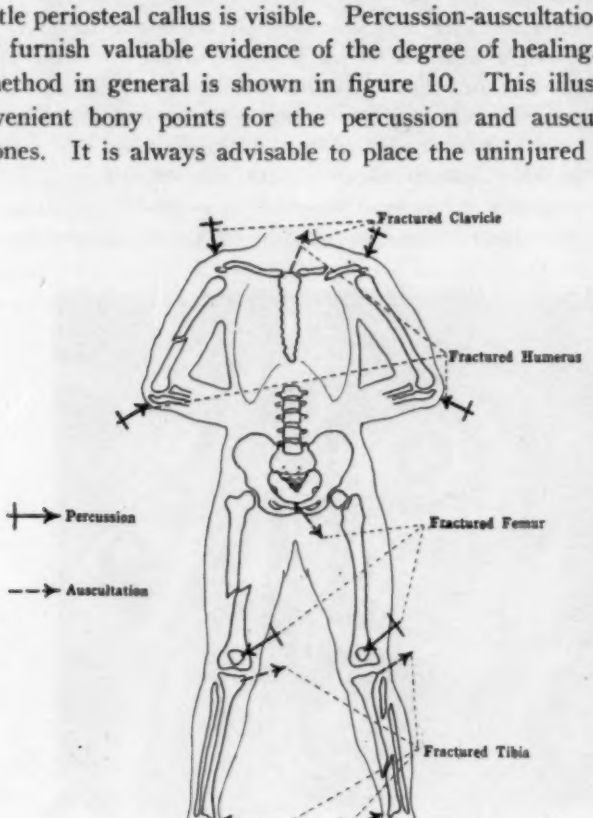


Fig. 10.—Points for percussion and auscultation.

in a symmetric position with the injured one. As stated before, traction on both extremities is sometimes advisable while the injured and control bones are being studied. When percussion and auscultation are used on the proximal long bones, it is always easier to place the stethoscope firmly on a central point, such as the symphysis pubis or the upper part of the manubrium. Then only the percussing finger needs shifting while the bell is held stationary; this eliminates extraneous noises. The clearest signs are elicited when a single bone is compared with its control normal bone. However, if there is much swelling over a percussion point, it is

better to shift to the next distal bony prominence on each extremity since the vibrations are readily transmitted through normal joints. Ordinarily a sharp, clean percussion stroke is used to set a large bone in vibration and to obtain normal resonance. However, a light minimal percussion just audible on the normal bone will at times show slight variations in intensity better than a heavy stroke. Since the distal two long bones in each extremity touch at each end, careful individual percussion must be carried out. The fingers may be studied by lightly tapping the ends and listening over the knuckles with a small bell. However, chip fractures and incomplete fractures cannot be diagnosed. The results are much more satisfactory in the large shaft fractures.

Confidence in this method comes only by experience. By listening to fractures before roentgenograms are made, one soon develops the practice so that it becomes more and more valuable. In percussing each fracture as it comes out of a plaster cast, one soon learns to anticipate the roentgen findings of healing and callus formation.

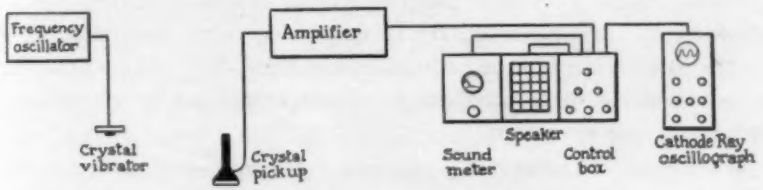


Fig. 11.—Apparatus used in this study.

The apparatus used in this study is shown in figure 11. The intensity or amplitude of the transmitted forced vibration and of the percussion note was thus recorded. This apparatus was frequently used likewise for demonstration before small groups so that the differences in the fractured extremity compared to the normal could be heard and seen. However, it should be strongly stressed that this elaborate apparatus is not at all necessary for clinical use. In fact, one of the virtues of this method of studying fractures is that no apparatus except a stethoscope is needed.

SUMMARY

Percussion-auscultation of bone is advocated as an aid in diagnosis, reduction and follow-up of certain shaft fractures, for it is simple, inexpensive and painless.

Changes in the percussion note due to the type of fracture, to the position of the fragments and to the degree of healing are described.

The late A. C. Seletzky, Ph.D., of the Case School of Applied Science, and Mr. John Murrary gave assistance in the technical problems involved in this study.

SOLITARY CONGENITAL (DYSONTOGENETIC) CYST OF THE PANCREAS

REPORT OF A CASE

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AND
L. J. STACY, M.D.
WHITE PLAINS, N. Y.

Solitary cyst of the pancreas has attracted widening interest among surgeons and pathologists, particularly during the last two decades. The number of cases reported in the medical literature testifies to the fact that this condition now must be considered relatively infrequent rather than rare of occurrence. These reports have added to our knowledge of the various clinical pictures of pancreatic cysts as well as of their surgical treatment. We are, however, far from a satisfactory understanding of the pathologic nature and the pathogenesis of these cysts. This deficiency is reflected in the many attempts to obtain a satisfactory classification of pancreatic cyst formation.

On the basis of the histologic picture, the differentiation is generally made between two main groups of pancreatic cysts: (1) true cysts, namely, those characterized by an epithelial lining of the cyst wall; (2) pseudocysts, or those in which an epithelial lining of the cyst wall is lacking.

The majority of pancreatic cysts are pseudocysts. The consensus is that pseudocysts are to be considered the end result of previous pathologic processes taking place in the pancreatic tissues as a result of, for example, inflammatory processes in the gland or that they are caused by external trauma followed by hemorrhages in the gland and the omental bursa.

The so-called retention cyst exhibits epithelial lining of the cyst wall and may be considered a true cyst. In its pathogenesis, however, it appears to resemble a pseudocyst. Pathologic processes in the gland, like pancreatitis or the formation of calculi, may be followed by retrogressive processes which in turn cause obstruction of the free flow of secretion, resulting in retention of secretion in one part of the gland; the inside lining will naturally consist of the epithelium of the now dilated ducts.

From the White Plains Hospital.

True cysts of other types are rare. They are (*a*) proliferating cysts (cystic adenoma, cystic epithelioma) and (*b*) congenital cysts.

Congenital cysts have attracted considerable attention in spite of their rarity for one particular reason, namely, their frequent combination with cysts in the liver, the kidneys, the lungs and the central nervous system. In his classic monograph on cerebellar cysts and angiomas of the retina, Lindau [1] stated that congenital cysts of the pancreas (dysontogenetic cysts) were present in more than half of the recorded cases of this particular condition of the central nervous system. He further concluded that congenital cysts of the pancreas, when encountered in the adult, are associated almost constantly with cysts of the central nervous system.

If substantiated, this concept of Lindau, for obvious reasons, must be of real significance, particularly to the surgeon specializing in abdominal operations. From an investigative point of view, however, it appears that even though in more than half of the recorded cases of pathologic change in the central nervous system dysontogenetic cysts of the pancreas were simultaneously exhibited, the reverse is not necessarily true, that is, the statistical picture might be altogether different when the percentage of central nervous system involvement in cases in which pancreatic cysts are the basis of the statistical material is computed. In order to arrive at a more definite concept of this relation, it therefore seems of some importance to encourage the report of all cases seen by neurologists or neurosurgeons, by surgeons specializing in abdominal operations and by pathologists.

On a previous occasion, Walters and one of us (K.K.N.) [2] reported a case of congenital cysts of the pancreas with partial pancreatectomy. A microscopic study of the removed specimen satisfied the requirements of dysontogenetic cysts of the pancreas. At that time (February 1936), a postoperative neurologic examination of the patient did not reveal any involvement of the central nervous system. A report of the improved condition of the patient, as found on her next and last return to the clinic (August 1936) was included in the report. A later communication from her home physician revealed that during the following year she was progressing well and gaining in weight; the urine remained sugar free and the patient had no digestive disturbances. In August 1937, she was operated on elsewhere because of an acute attack of appendicitis,

1. Lindau, A.: Studien über Kleinhirncysten. Bau, Pathogenese und Beziehungen zur Angiomatosis retinae, Acta path. et microbiol. Scandinav., 1926, supp. 1, pp. 1-128.

2. Nygaard, K. K., and Walters, W.: Polycystic Disease of the Pancreas (Dysontogenetic Cysts): Report of Case with Partial Pancreatectomy, Ann. Surg. **106**:49-53 (July) 1937.

after which she apparently made an uneventful recovery. About January 1938, or two years after the partial pancreatectomy, she had noted the onset of general weakness, a sensation of epigastric fulness and some increase in the size of the remaining abdominal tumors. There were no further reports of the patient's condition until she died during the latter part of 1938.[3]

We have recently had an opportunity to see a patient who presented a picture similar to that in the case just mentioned, in that no pathologic changes of the central nervous system were demonstrable. The pancreatic cyst, however, was unilocular and obviously of a different category than the polycystic formations, although the condition in both cases was evidently congenital. For these reasons a brief communication is of interest.

REPORT OF CASE

A woman 35 years of age was first seen by us on June 25, 1941. About four or five weeks previously, on placing her hand over the upper part of the abdomen, she felt a movable lump under the left costal margin. She did not know whether it had been present long since she never before had had any symptoms referable to the abdomen and had never had a careful physical examination. After she had noted the abdominal lump she occasionally felt a slight soreness or dragging sensation in the upper part of the abdomen, particularly on changing from side to side while recumbent. After detecting the lump, she had not noted any increase in its size. Aside from this information, her past and present history was not significant.

Physical Examination.—The patient was of the asthenic type; she was rather high strung but appeared to be in good general condition. Her blood pressure was 110 systolic and 86 diastolic. With the patient in the recumbent position, a moderately large rounded prominence was noted in the upper left quadrant of the abdomen. Dulness was present over this area. Palpation revealed an intra-abdominal tumor, well circumscribed, not tender and freely movable from side to side but less so in the longitudinal axis of the body. The tumor also moved moderately with respiration. When the patient lay on her right side, the tumor could be felt to the right of the midline. At the same time, she experienced a dragging sensation deep in the left upper quadrant of the abdomen. The physical examination otherwise gave essentially negative results.

Laboratory Investigation.—The concentration of hemoglobin was 12 Gm. per hundred cubic centimeters of blood. Erythrocytes numbered 4,400,000 and leukocytes 8,000. The differential count was normal; urinalysis also gave normal results. In the complement fixation tests for syphilis, a titer of more than 10 was obtained. An excretory urogram revealed moderate ptosis of the right kidney; the left kidney was in normal position. Otherwise, the outlines of the kidneys, the kidney pelves and the ureters were normal, with good excretion of contrast medium on both sides after five minutes.

The preoperative diagnosis was cyst of the mesentery, omental cyst or pancreatic cyst, in the order mentioned.

Operation.—An exploratory laparotomy was performed on July 1 by one of us (K. K. N.). Palpation of the right and left kidneys did not reveal cysts. In the

3. Walters, W.: Personal communication to the authors.

dome of the liver, four small cyst formations were noted, the largest of these measuring 5 mm. in diameter.

The palpable tumor was protruding behind the gastrocolic ligament as well as behind the transverse mesocolon. Because of its intimate contact with the larger vessels of the transverse mesocolon, the tumor was exposed through an opening

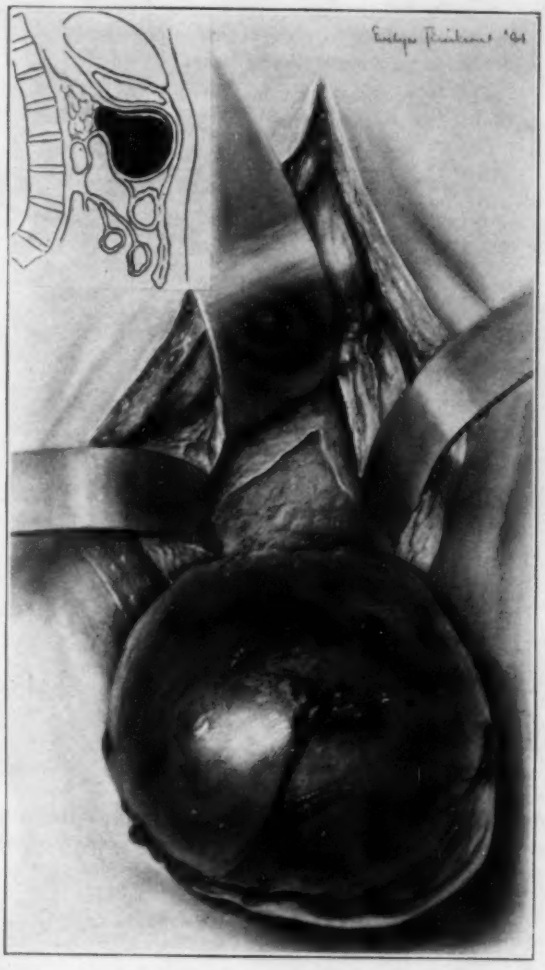

Fig. 1.—Drawing illustrating a pancreatic cyst originating from the lower border of the pancreas. In the inset is shown the operative finding in the sagittal section.

made in the gastrocolic ligament. It was dissected free from its connection with the transverse mesocolon. The tumor was fluctuating. It originated with a rather broad pedicle of normal-appearing pancreatic tissue from the lower border of the body of the pancreas (fig. 1). By careful dissection of its pedicle, it was possible

to peel the intact cyst out of its connection with the pancreatic tissues, leaving a concave area in the pancreas into which the base of the cyst could be fitted like an egg into an eggcup. The bleeding points of the glandular tissue were carefully clamped and tied with silk sutures. Exploration of the pancreas did not reveal the presence of other observable or palpable pathologic processes. Exploration of the other abdominal organs revealed nothing of essential importance. The opening in the gastrocolic ligament was closed around two Penrose drains, inserted down to the area of dissection to prevent the accumulation of the unavoidable postoperative secretion of pancreatic tissue juices.

Pathologic Report.—The intact cyst measured 7 by 8 by 8 cm. and weighed 193 Gm. It was unilocular and contained pale yellow clear fluid. The wall of the

Fig. 2.—Photomicrograph of the cyst wall showing the internal lining composed of a single layer of low cuboid epithelium with a single layer of columnar epithelium covering a teatlike projection in a papillomatous area. Note the pancreatic tissue in the lower left corner.

cyst was 0.5 mm. thick. Its inner surface was smooth with the exception of a teatlike projection 3 mm. in diameter and 4 mm. long.

Microscopic examination showed that the cyst wall was formed by stretched connective tissue lined by a single layer of cuboid epithelial cells, except that the filiform projections in the papillomatous area were covered with a single layer of columnar epithelium. Corresponding to the part of the cyst attached to the pancreatic pedicle were areas of pancreatic tissue that contained scattered islands of Langerhans, all of which appeared normal (fig. 2). Chemical investigation of the cyst fluid revealed a diastatic activity of 5,333 units and a tryptic activity of 100 units (Gross' method) as well as lipase.

Postoperative Course.—The patient's immediate reaction to the operation was moderate and her further course uneventful. During the first postoperative week,

drainage from the wound had a mild digestive activity on the skin surrounding the drains. These were removed on the ninth postoperative day, and the wound had entirely healed with no further drainage after the sixteenth day.

A dextrose tolerance test performed two weeks after operation gave essentially normal results. In view of the nature of the cyst, a careful neurologic examination was performed before the patient left the hospital. No pathologic changes of the central nervous system could be found. Up to the time of writing, her further course has been satisfactory. Antisyphilitic treatment was started as soon as she had recovered sufficiently from the operation.

COMMENT

In most cases of cysts of the pancreas, the whole diagnostic armamentarium of the clinician has to be mobilized. Only in this way may it be possible for him to arrive at an accurate diagnosis which will enable the surgeon confidently to plan a surgical approach and which will enable both to form an opinion of what may and may not be expected from the operation so far as its therapeutic results are concerned. Three types of symptoms should be kept in mind, namely: (1) symptoms referable to the presence of the intra-abdominal tumor; (2) symptoms referable to the presence of pathologic processes which in turn have led to the formation of pancreatic cysts (trauma with hemorrhage into the omental bursa, pancreatitis, cholecystitis, cholelithiasis), and (3) coincidental symptoms caused by independent pathologic processes in the other abdominal organs. In the presence of dysontogenetic cysts, a fourth type of symptoms also should be kept in mind, namely, symptoms referable to cyst formations in other intra-abdominal as well as extra-abdominal organs.

In the present case, this diagnostic difficulty was in no way illustrated. With the verification of the presence of an intra-abdominal tumor without other significant symptoms, exploratory laparotomy suggested itself.

The free mobility of a tumor in the upper part of the abdomen admittedly does not preclude the presence of pancreatic cysts. In 47 cases reported by Judd and associates,[4] free mobility was encountered in 11 of the cases, with 9 of these originating in the tail of the pancreas. In our preoperative discussion of the diagnosis, we placed pancreatic cyst as the last of the likely possibilities because of the extreme mobility. The operative findings satisfactorily explained this sign.

The real interest in the present case centers on the pathologic nature of the cyst. The presence of all three enzymes, namely, diastase, trypsin and lipase, together with the operative findings, indicates the pancreatic origin of the cyst. The endothelial lining indicates the true cystic nature. The absence of other observable or palpable pathologic changes of the pancreas seems to exclude the possibility of a retention cyst.

4. Judd, E. S.; Mattson, H., and Mahorner, H. R.: Pancreatic Cysts: Report of Forty-Seven Cases, Arch. Surg. **22**:838-849 (May) 1931.

Finally, the simultaneous formation of cysts in the liver coupled with the deductions already made favors the assumption that we had here a type of dysontogenetic cysts localized in the pancreas and the liver. Recalling the positive serologic test for syphilis, it seems difficult to picture these findings resulting from latent syphilis.

The dysontogenetic cysts of the pancreas are described as having a characteristic histologic picture. Smaller or larger cysts are distributed throughout the entire gland without circumscribed localization. The interstitial tissue is greatly increased, thereby reducing the parenchymatous tissues which otherwise exhibit a normal picture with intact islands of Langerhans. The cyst wall is lined with cuboid epithelium, except in areas with cylindric cells covering papillary proliferations of the cyst wall protruding into the lumen of the cyst.

On the basis of this characteristic picture, earlier pathologists (Wegelin, Yamane, Priesel)[5] conceived the origin of these cysts as a developmental anomaly. For this reason, the growths were termed dysontogenetic cysts. According to Yamane, the earliest developmental anomaly led to isolation of small pancreatic ducts, which partly by retention of glandular tissue secretion, partly by uncoordinated growth of the epithelium, subsequently gave rise to multiple cyst formation. It is of interest to note that the theory of cyst formation implies the polycystic nature of the developmental anomaly.

In one essential respect the cyst reported did not correspond to the characteristic picture of dysontogenetic cysts. It was a solitary unilocular cyst and was not polycystic. In this connection, it is of interest to note that Gruber[6] admitted the rare finding of solitary unilocular dysontogenetic cysts. It is further to be noted that with regard to the microscopic picture of its endothelial lining, the present cyst exhibited a picture identical to that of the individual cyst of polycystic formations. Finally, the simultaneous cyst formations in the liver have to be kept in mind. It is of significance to note that Ledebur[7] many years ago maintained that the developmental origin of polycystic disease of the pancreas could be considered definite only in case of simultaneous cysts in the liver or the kidneys. Although this contention subsequently has been refuted, such a multiple localization of cysts, when present, constitutes added evidence of its congenital origin. In conclusion, therefore, it seems justified to report this present case as representing an unusual type of dysontogenetic cyst located in the pancreas and the liver.

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5. Wegelin, Yamane and Priesel, cited by Lindau.[1]

6. Gruber, G. B.: Pathologie der Bauchspeicheldrüse (Mit Ausnahme der Langerhansschen Inseln und der Diabetesfrage), in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1929, vol. 5, pt. 2, pp. 211-621.

7. Ledebur, cited by Gruber.[6]

MANAGEMENT OF RUPTURE OF THE UTERUS

REPORT OF FORTY-FOUR CASES

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Of the complications of pregnancy and labor, rupture of the uterus is one of the most dangerous.

The object of this communication is to present what informative data are available from a study of 44 patients with rupture of the uterus treated in the Peiping Union Medical College Hospital. This study is especially concerned with the treatment of this condition. Although the available literature has been consulted, an exhaustive review is not attempted. The case histories, illustrative of conditions of obstetric practice in this part of the world, are reported briefly.

Some problems, such as those caused by osteomalacia, which although common here, is rare elsewhere, are peculiar to this region. One may gain an impression also of the obstetric problems arising in a community in which many of the deliveries are attended by untrained midwives without the slightest idea of asepsis or of the mechanism of labor. Through the years there has been a gradual and definite decrease in the mortality rate for those treated for rupture of the uterus in the Peiping Union Medical College Hospital; after analysis of our material, certain factors seem to stand out to explain the improvement. These are: improvement in the availability of blood for transfusion; uniformity in the surgical management in these cases; the benefit of chemotherapy; the advantages of decompression of the gastrointestinal tract, when indicated, by continuous suction on the principle of the Wangensteen apparatus.

Estimates of the frequency of this condition are misleading. There were only 8 instances of rupture of the uterus in this hospital from 1922 to 1934; these were reported by Eastman [1] and Wang.[2] There were 44 of these accidents from 1934 to July 1941. This marked increase in the hospital incidence is probably due to the growing willingness of

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1. Eastman, N. J.: Am. J. Obst. & Gynec. **11**:500, 1926.
2. Wang, A.: Nat. M. J. China **21**:121, 1935.

the general population to accept hospital treatment. Since there were 52 patients in all with rupture of the uterus among 11,500 obstetric admissions in the history of this department, the incidence in this hospital is 1 in 220. If only the years 1934 to 1941 (the time during which the 44 cases hereinafter reported occurred) are considered, the frequency is 1 in 95. Only 6 of these accidents occurred among our own antepartum patients, while 38 were accepted as emergency cases. The incidence in reports from American and European hospitals varies from 1 in 255 deliveries to 1 in 2,000. We are reporting the highest incidence of this condition that has come to our attention.

Deductions as to the frequency in relation to the number of deliveries in the community are unsatisfactory; this can be said of much statistical data obtained from hospitals admitting many emergency cases.

All of these women unless otherwise indicated were Chinese.

RUPTURE OF THE UTERUS DURING LABOR DUE TO MATERNAL CAUSES

RUPTURE OF THE UTERUS DUE TO A CONTRACTED PELVIS

CASE 1.—C. L. P., aged 41, a septipara in her eighth pregnancy with the expected date of confinement in June 1935, was admitted on July 1 in labor of five hours' duration. She had been examined repeatedly by a midwife. The patient had had symptoms of osteomalacia since her fifth pregnancy, six years previously. All previous deliveries had been spontaneous and easy. On admission, the patient was in shock and the fetal heart was not heard. The abdomen was tender, and the pelvis was deformed by osteomalacia with a transverse outlet of 6.5 cm. Rupture of the uterus was evident. When the abdomen was opened, the fetus and the placenta were in the abdominal cavity, and a tear which extended through the left broad ligament and the vaginal wall was found in the lower uterine segment. Subtotal hysterectomy was done, and a blood transfusion was given during the operation. The condition of the patient was poor during the operation, but recovery was uneventful, and she was discharged on the twentieth day in good condition.

CASE 2.—C. W. H., aged 19, was admitted in her first pregnancy on Feb. 15, 1936, three weeks from term with ruptured membranes. She had been in labor for three days. The patient had been examined repeatedly by a midwife. Regular labor pains had stopped for twenty-four hours. On admission, the patient was in shock with vomiting and air hunger, and the abdomen was rigid and tender. No fetal heart was heard. The pelvis was markedly deformed by osteomalacia with a transverse outlet of 3 cm. When the abdomen was opened, free blood gushed out. The uterus was ruptured across the anterior portion of the cervix through the right broad ligament, and the shoulder of the fetus protruded through the tear. Subtotal hysterectomy was done. A blood transfusion was given during the operation, but the patient died seven hours later.

CASE 3.—C. S. K., aged 20, a secundipara in her third pregnancy, was admitted on March 8, 1937, two weeks from term, in labor of thirty hours' duration. She had been examined by a midwife. The first baby had been born spontaneously; the second had been delivered with difficulty by breech extraction three years

before admission. The patient had had symptoms of osteomalacia for three years. On admission, the abdomen was tender; the cervix was fully dilated. The fetal parts were felt superficially; the heart tones were not heard. The pelvis was deformed by osteomalacia. At operation, the placenta and the fetus were found in the abdominal cavity. There was a rupture of the uterus from the anterior vaginal fornix extending transversely to both sides. Subtotal hysterectomy was done. She died on the eighth day after a stormy postoperative course.

CASE 4.—W. L. C., aged 32, a secundipara in her third pregnancy, was admitted two weeks from term on July 8, 1937, in labor of thirty-five hours' duration. The membranes were ruptured, and regular labor pains had ceased for eighteen hours. She had been examined by a midwife. The patient had had symptoms of osteomalacia for three years. Previous deliveries were spontaneous and easy; the last had been four years before. On admission, the patient looked extremely sick and had constant abdominal pain. The pelvis, the spinal column, the chest and the extremities were markedly deformed by osteomalacia. No fetal heart was heard; the fetal parts were felt superficially. There were signs of generalized peritonitis. Subtotal hysterectomy was done; about 1,000 cc. of blood was removed from the abdominal cavity, and a blood transfusion was given. The uterus had been torn in the right lower segment, and one fetal arm and shoulder protruded into the abdominal cavity. She died nineteen hours after admission. Autopsy showed generalized peritonitis and streptococcic septicemia.

CASE 5.—P. C. C., a chondrodystrophic dwarf aged 33, was admitted in her first pregnancy on Nov. 5, 1937, one week past term, after being in labor for twenty hours and with rupture of the membranes for twelve hours. She had been repeatedly exmained by a midwife, and there had been a sudden sharp abdominal pain with stoppage of regular labor pains and fetal movements. On admission, the patient was in shock, and the abdomen was tender. The fetal parts were felt superficially, and no fetal heart was heard. Vaginal examination revealed a uterine tear over the left side. The patient had a flat pelvis, and the diagonal conjugate diameter measured 10.5 cm. When the abdomen was opened, a moderate amount of blood was present in the peritoneal cavity, together with the baby and the placenta. The tear extended from the left vaginal fornix through the left broad ligament. Subtotal hysterectomy was done. The patient had a septic postoperative course with paralytic ileus and pulmonary complications which terminated in death on the eighth day.

CASE 6.—Y. Y. H., aged 37, a quartipara in her fifth pregnancy, was admitted on Feb. 24, 1938, at term. The membranes had ruptured spontaneously; this was followed by prolapse of a fetal arm. The patient replaced the arm herself, but after eight hours of labor, the arm again prolapsed, and she came to the hospital. On admission she was found to have a generally contracted pelvis with a diagonal conjugate diameter of 10.25 cm. The fetal heart was not heard. Decapitation was done; after this an incomplete transverse tear in the anterior wall of the lower uterine segment was found. The uterus was packed and a blood transfusion given. The family insisted on taking the patient home, and she died the following day.

CASE 7.—Y. S. T., aged 24, a secundipara in her third pregnancy, was admitted at term on June 21, 1938, after a labor of eleven hours and with rupture of the membranes of five hours. She had been examined by a midwife. She had a history of osteomalacia of six years' duration, and the previous labors had been difficult. On admission, the patient was in shock; the fetal head was above the pelvic inlet,

and the heart tones were absent. The pelvis was deformed by osteomalacia. Vaginal examination was done, and a tear over the lower uterine segment toward the right was found. A blood transfusion was given before the operation. When the abdomen was opened, the baby and the placenta were free in the peritoneal cavity. There were signs of peritonitis. The rupture was in the lower uterine segment and involved the right side and the whole anterior surface. Subtotal hysterectomy was done, and another transfusion was given. The patient died five hours after the operation. A postmortem blood culture demonstrated the colon bacillus.

Case 8.—L. C. H., aged 27, a tertipara in her fourth pregnancy, was admitted on June 18, 1939, two weeks past term. She had been in labor for twenty hours; the membranes had ruptured, and the cord was prolapsed. She had been examined by a neighbor. The first child had been born spontaneously. The second labor was prolonged and was terminated by a destructive operation done by a midwife. The third child was stillborn. On admission, the patient was in shock; the abdomen was tender, and the fetal heart was not heard. The pelvis was deformed by osteomalacia, with a transverse outlet of 7 cm. and a diagonal conjugate diameter of 9 cm. The baby was delivered by breech extraction. Vaginal examination done after delivery revealed a rupture of the uterus. At operation, the uterus was found torn anterolaterally toward the left. Subtotal hysterectomy was done. A blood transfusion was given during, and another after, the operation. The postoperative course was uneventful, and the patient was discharged twenty-six days later.

Case 9.—W. T. M., aged 28, a secundipara in her third pregnancy, was admitted at term on Sept. 3, 1939, after being in labor for sixty hours and with rupture of the membranes for four days. The labor pains had stopped, and the patient had been mentally cloudy for ten hours. Attempts by a midwife to bring about delivery had been unsuccessful. The first two deliveries had been spontaneous; the last of these was four years before admission. She had had bone pains for three years. On admission, the patient was in shock; the uterus was in tetanic contraction, and no fetal heart was heard. The pelvis was deformed by osteomalacia, with a transverse outlet of less than 6 cm. Craniotomy was done with great difficulty. The uterus was later found to be ruptured, and a blood transfusion was given before the operation. At operation, the uterus was found torn on the left side up to the broad ligament. Subtotal hysterectomy was done. The patient died four hours after admission.

Case 10.—L. H. W., aged 22, a secundipara in her third pregnancy, was admitted at two weeks from term on Nov. 11, 1939, after being in labor for three days with rupture of the membranes for thirty-three hours. The patient had been examined repeatedly by a midwife. Labor pains had stopped for eight hours, and the patient had become mentally cloudy and restless. Her history suggested that she had had osteomalacia for the past four years. On admission, the patient was in a moribund state. Material with the appearance of coffee grounds flowed from the mouth. The fetal parts were felt superficially, and shifting dulness was demonstrated. No fetal heart was heard. Generalized tenderness was present over the abdomen. The pelvis was deformed by osteomalacia. Dextrose infusion followed by a blood transfusion was given. Flatus escaped when the abdomen was opened. The baby was on top of the uterus, which was torn anteriorly over the lower uterine segment. The posterior wall of the bladder was completely torn. There were extensive

peritonitis and paralytic ileus. Subtotal hysterectomy was done, and no attempt was made to repair the bladder because of extensive necrosis. Another blood transfusion was given after the operation. The patient died eleven hours after admission. At autopsy acute general peritonitis was found.

CASE 11.—S. K. L., aged 29, a quartipara in her fifth pregnancy, was admitted ten days before term, on Nov. 24, 1939, after being in labor for fifteen hours without making progress. The patient was referred here from another institution because of an attack of severe pain an hour prior to admission. On admission, the patient was in shock; the fetus was in the abdominal cavity, and the pelvis was deformed by osteomalacia. At operation, free blood, the fetus and the placenta were found in the peritoneal cavity. The rupture of the uterus was on the right side in the lower uterine segment. Subtotal hysterectomy was done, and a blood transfusion was given during and after the operation. The postoperative course was stormy; the abdominal wound was infected, and a pelvic abscess developed, which was drained. The patient recovered and was discharged forty-four days after the operation.

CASE 12.—J. K. M., aged 33, a primipara in her second pregnancy, was admitted a week from term, on July 12, 1940, after being in labor for eleven hours. The patient was referred here from another institution. The membranes had ruptured spontaneously six hours before admission. A vaginal examination had been done by a physician at the other institution, and the fetal head was found to be floating above the pelvic inlet in spite of the strong uterine contractions. On admission, the fetus was in left occipitoanterior position with the presenting part above the spines. The fetal heart tones were good. The cervix was 6 to 7 cm. dilated, and the uterine contractions were strong. The patient was found to have a generally contracted pelvis with a diagonal conjugate diameter of 10 cm.; the transverse outlet measured 6.5 cm. When the abdomen was opened, a partial rupture of the uterus was found with two large subperitoneal hematomas, one on each side of the uterus. Subtotal hysterectomy was done, and the baby lived. A blood transfusion was given after the operation. The postoperative course was uneventful, and the patient left the hospital after twenty days.

RUPTURE OF THE UTERUS THROUGH AN OLD CESAREAN SECTION SCAR

CASE 13.—K. H J., aged 34, a primipara in her second pregnancy, was admitted on Sept. 11, 1934, six weeks before the expected date of confinement because of sudden acute abdominal pain followed by collapse. She had undergone a classic cesarean section in this hospital in 1931 because of a generally contracted pelvis; the postoperative course had been febrile. On admission, the abdomen was tender, but the patient's condition was relatively good. At operation the shoulder of the baby was found to be protruding through the old uterine scar. The baby was delivered in good condition, and the tear was repaired. The patient was discharged in good condition in twenty days.

CASE 14.—U. L., a Russian housewife aged 30, a primipara in her second pregnancy, was admitted on Nov. 2, 1940, two weeks before the expected date of confinement. She had had a classic cesarean section in 1938 in another hospital because of abruptio placentae. The abdominal wound was badly infected but healed in three months. On admission, the patient had been in labor for twenty-four hours and had ceased to make progress. There was some abdominal pain, and operation

was decided on. When the abdomen was opened, a rupture through the old scar was found. The dead fetus was extracted, and subtotal hysterectomy was done. The patient left the hospital in fifteen days after an uneventful course.

CASE 15.—L. L. C., aged 33, a secundipara in her fourth pregnancy, was admitted in labor a month from term, on June 7, 1941. The patient had had two classic cesarean sections in 1936 and 1939, respectively, because of a funnel pelvis. On the day before admission, the patient complained of intermittent pain in the lower part of the abdomen which continued and became severe. On admission the patient was in good condition. Labor pains occurred every few minutes, and a cystic mass became palpable in the lower part of the abdomen during each pain. There was tenderness over the abdominal scar. The fetal heart tones were good. Rupture of the uterus was diagnosed. At operation there was found a complete separation of the old scar. The membranes were intact and were bulging out of the uterus during the pains. The live baby was extracted and the old scar repaired. The patient made an uneventful recovery and was discharged fifteen days later.

RUPTURE OF THE UTERUS DUE TO TRAUMA

CASE 16.—L. C. L., aged 41, a quintipara in her sixth pregnancy, was admitted on Oct. 14, 1935. She had been in labor with ruptured membranes for fifteen hours. During this time, a midwife had tried to effect delivery by pushing on the fundus of the uterus. The previous deliveries had been uneventful. On admission, the patient was in desperate condition with a pulse rate of 140 and generalized abdominal tenderness. The fetal heart was not heard. During the preparations for craniotomy, a tear in the lower uterine segment was discovered. At operation, the fetus was found in the peritoneal cavity, and there was a tear through the lower uterine segment extending to the left lateral pelvic wall. Subtotal hysterectomy was done, and the patient died before supportive measures could take effect.

CASE 17.—C. L. F., aged 32, a tertipara, was admitted on March 13, 1937, two weeks past the expected date of confinement, because of high fever two days after delivery. The baby had been delivered stillborn with forceps; after this, the placenta had been manually removed. The previous deliveries had been uneventful. On admission, the patient was extremely sick and was treated for puerperal sepsis. Six days after admission, a cystic mass was felt in the abdomen. At operation, old blood was removed from the peritoneal cavity. A small rupture in the anterior wall of the uterus and a mass of matted bowel were not disturbed. The wound was drained, and patient recovered and was discharged twenty-three days after the operation.

CASE 18.—W. C. C., aged 36, a quintipara in her sixth pregnancy, was admitted at term on Nov. 21, 1937. A midwife had ruptured the membranes early in labor, the duration of which had been twenty-six hours. Eleven hours before admission, the midwife had tried to hasten delivery by pressure on the fundus of the uterus; during this procedure, the patient had a sudden sharp pain, and regular uterine contractions ceased. The previous deliveries were uneventful, and the pelvic measurements were normal. On admission, the patient was in shock; the abdomen was tense and tender, and the fetal parts were easily felt. The fetal heart tones were not heard. At operation, the fetus and the placenta were free in the abdominal cavity, and the rupture extended transversely across the lower uterine segment. Subtotal hysterectomy was done, and a blood transfusion was given during the operation. The postoperative course was relatively smooth, and the patient was sent home thirty days later.

CASE 19.—L. T. H., aged 39, a quartipara in her fifth pregnancy, was admitted on Nov. 21, 1938, two weeks before the expected date of confinement. Subtotal thyroidectomy had been done several years previously; after this tetany developed requiring calcium treatment. She also had chronic interstitial nephritis. The patient had been admitted at six months' gestation because of hypertension and retinal hemorrhage. Her condition improved, and she was allowed to go home. She was admitted in labor, which progressed satisfactorily for twelve hours; at the end of this time, the cervix was completely dilated, and the fetal head was seen at the vulva. Her general condition was good. A physician tried to assist delivery by pushing on the fundus of the uterus during a uterine contraction. The pains ceased, the fetal head receded, and the patient went into a state of collapse. A blood transfusion was given during the operation. The baby was dead in the peritoneal cavity, and the rupture extended obliquely through the right side of the lower uterine segment. Subtotal hysterectomy was done. The patient made a smooth recovery and was discharged on the twenty-fourth day after the operation.

RUPTURE OF THE PREGNANT HORN OF A BICORNUATE UTERUS

CASE 20.—C. C. F., aged 21, was referred to the Peiping Union Medical College Hospital in her first pregnancy on Dec. 29, 1936, near term. The patient was said to have been in labor for three days when labor ceased. After several days, the physician thought it best to induce labor by the introduction of a bougie and found that the uterus seemed to be empty. The condition of the patient was good, and rupure of the uterus was not suspected. On admission, the baby was superficially felt; the fetal heart was not heard, but there was no abdominal tenderness. At operation, the dead fetus was found in the abdominal cavity. The whole summit of the left horn of the bicornuate uterus had ruptured. The right horn was the size of a hen's egg. The enlarged left horn was removed, and the patient made an uneventful recovery.

RUPTURE OF THE UTERUS DUE TO UNKNOWN CAUSES

CASE 21.—L. S. Y., aged 29, a secundipara in her third pregnancy, was admitted at term on Nov. 1, 1935. During her nine hour labor, she had been examined by a midwife. The fetal head had been seen at the vulva but had now receded, and the patient had fainted. Her first two deliveries had been easy. On admission, the patient was in shock; the fetal heart was not heard, and there was much abdominal tenderness. By vaginal examination, the fetal arm and a tear in the anterior wall of the lower uterine segment could be felt. A blood transfusion was given, and at operation the fetus and the placenta were found free in the abdominal cavity. There was a complete rupture through the right lateral wall of the uterus. Subtotal hysterectomy was done, and after a stormy course she was sent home on the thirty-sixth day after the operation.

CASE 22.—L. P. M., aged 32, a sextipara in her seventh pregnancy, was admitted two days from term on Nov. 9, 1936, in labor for forty-eight hours and with ruptured membranes for twenty-four hours. The patient had been manipulated by a midwife. The previous deliveries had been spontaneous and easy. On admission, the patient was exhausted and dehydrated. The abdomen was tender, and the fetal parts were felt superficially. No fetal heart was heard. The pelvis was of the funnel type. On opening the abdomen, the fetus and the placenta were free in the abdominal cavity. The uterus was ruptured anteriorly through the left side to the left broad ligament and from the cervix into the vagina. Total hysterectomy was done.

Blood was given after the operation. The next day, the abdomen became much distended, and the patient had a chill and a high fever, followed by unconsciousness. She died forty-one hours after admission.

CASE 23.—L. J. S., aged 45, an undecimipara in her twelfth pregnancy, was admitted on Sept. 4, 1937, one week past term. She had been in labor for three days. The membranes were ruptured, and regular pains had ceased for seventeen hours. A midwife had made many examinations. Previous deliveries had been uneventful. On admission, the patient was in shock. There was moderate vaginal bleeding; no fetal heart tones were heard; the abdomen was tender, and the fetus was easily palpable. On vaginal examination, a tear in the anterior vaginal wall was found, but the fetus could not be reached. When the abdomen was opened, the fetus, the placenta and much old blood were found in the peritoneal cavity. Subtotal hysterectomy was done, and a blood transfusion was given. The patient died of peritonitis eleven hours after the operation. Hemolytic streptococci was demonstrated by a blood culture.

CASE 24.—C. T. S., aged 25, a primipara in her second pregnancy, was admitted at term on June 20, 1940, in labor complicated by dysentery. The pelvic measurements were normal, and there was a scar in the posterior vaginal wall, probably a result of the previous delivery. The fetal head failed to engage in the pelvic inlet, and after active labor of seventeen hours' duration and when the cervix was 8 cm. dilated, the fetal heart tones disappeared, and there was constant abdominal pain. The patient was operated on immediately, and the dead baby and the placenta were found in the peritoneal cavity. There was a large tear across the anterior surface of the lower uterine segment, extending into the left broad ligament. Subtotal hysterectomy was done, and a blood transfusion was given during the operation. Recovery was smooth.

RUPTURE OF THE UTERUS DURING LABOR DUE TO FETAL CAUSES

RUPTURE OF THE UTERUS DUE TO TRANSVERSE PRESENTATION OF THE FETUS

CASE 25.—L. Y. H., aged 25, a quintipara, was referred from another institution on Aug. 30, 1934, because of abdominal pain for one day following delivery. The fetus had presented transversely. After failure of an attempt at decapitation, the baby had been delivered by podalic version and extraction. The patient was sent to the Peiping Union Medical College Hospital in shock. There was generalized abdominal tenderness, and complete rupture of the uterus was found on vaginal examination. At operation, the tear was found to extend through the left broad ligament midway to the fundus. Subtotal hysterectomy was done, and a blood transfusion was given. She died twenty-four hours after admission. Autopsy showed general peritonitis, myometrial abscess and hemolytic streptococcic septicemia.

CASE 26.—L. T. L., aged 34, a duodecimipara in her thirteenth pregnancy, was admitted on May 7, 1935, two weeks past term. She had been in labor for thirty-two hours, and a fetal arm had been prolapsed for eight hours. There had been repeated attempts on the part of a midwife to effect delivery. The previous obstetric history was not significant. There was generalized abdominal tenderness, and a decapitation was done with difficulty. The abdomen became distended, and profuse bleeding, arterial in character, appeared on the fifth day post partum. A blood transfusion was given and the uterus packed, but the patient died. Clostridium welchii was obtained from the culture taken from the uterus.

CASE 27.—P. Y. C., aged 32, a quartipara in her fifth pregnancy, was admitted on March 25, 1936, after a labor of seven hours' duration. A fetal arm and the cord had been prolapsed for three hours, and attempts of a midwife to deliver the baby had been unsuccessful. The previous deliveries had been spontaneous. On admission, the patient was in shock; the pulse rate was 130 and poor in quality; the abdomen was tender, and the fetal heart tones were not heard. Delivery was effected by decapitation. After this, two tears in the cervix were found; the one on the right extended into the broad ligament. Repeated blood transfusions were of no avail, and the patient died four days later. A blood culture yielded a growth of hemolytic streptococci.

CASE 28.—C. C. C., aged 34, a tertipara in her fourth pregnancy, was admitted on June 21, 1937, two weeks past term. She had been in labor for six hours, and the membranes had been ruptured for three hours; this was followed by prolapse of a fetal arm. A midwife had tried to deliver the baby by pulling on the arm. The fetal heart tones were absent. Decapitation was done. A tear in the lower uterine segment was found through which part of the intestine was felt. The family refused to allow operation and took the patient home. A social worker has since reported that the patient is living and well.

CASE 29.—T. H. Y., aged 34, a tertipara in her fourth pregnancy, was admitted on Dec. 30, 1937, two weeks before term. She had been in labor for sixteen hours, and the fetal arm had been prolapsed for six hours. Previous deliveries had been uneventful. She had had severe abdominal pain on the day before admission and was examined by a neighbor. On admission, the patient was restless; the pulse was weak and poor in quality, and the temperature was 38.5 C. (101.3 F.). The abdomen was tender; the fetal heart was not heard, and the uterus remained in tetanic contraction. Decapitation was done; after this, a complete rupture of the uterus through the left broad ligament was discovered. On opening the abdomen, general peritonitis was evident. Subtotal hysterectomy was done, and the patient died three days later.

CASE 30.—L. C. M., aged 33, a sextipara in her seventh pregnancy, was admitted on Feb. 9, 1938, two weeks before term. Labor had been in progress for two days. The membranes had been ruptured for ten hours and a fetal arm prolapsed for eight hours. Regular pains had ceased; the patient had become pale and restless and had examined herself. On admission, the patient was in shock; the fetal heart was not heard; the fetus was superficially felt, and shifting dulness was demonstrable. There was a spurt of flatus as the abdomen was opened. Complete rupture through the left broad ligament was found, but the fetus was still in the uterus. Subtotal hysterectomy was done, and the patient died sixteen hours after admission. Two blood cultures were obtained and both showed beta hemolytic streptococci.

CASE 31.—H. S. K., aged 35, a septipara, was admitted on Dec. 27, 1939, one week past term, because of severe abdominal pain for two days after delivery. The baby had been in transverse presentation and was extracted by a physician. The placenta was also manually removed. After delivery, there was abdominal pain, fever, nausea and vomiting. On admission, the patient was unconscious; the temperature was 38.6 C. (101.4 F.), and the pulse rate was 150. There were generalized boardlike rigidity over the abdomen, petechia over the skin and signs of pneumonia. A blood transfusion was given, but the patient died five hours after admission.

Shigella paradysenteriae of the mannite-fermenting group was demonstrated in a blood culture. A postmortem pelvic examination revealed a tear in the lower uterine segment extending into the left broad ligament.

CASE 32.—L. F. S., aged 44, a nonipara, was admitted on Jan. 3, 1940. She had been in labor for three days and was repeatedly examined by a midwife. She had been admitted to another hospital, where decapitation was done because of the death of the baby and the prolapse of the fetal arm. It was then found that there was a rupture of the posterior wall of the uterus, and the patient was referred to this hospital. The diagnosis was confirmed, and with the patient in relatively good condition, subtotal hysterectomy was done. The rupture extended through the posterior and left wall of the cervix. The lower uterine segment and both the anterior and the posterior leaf of the left broad ligament were torn. A blood transfusion was given during and after the operation. Signs of peritonitis and bronchopneumonia soon appeared, and the patient died fifty hours later.

CASE 33.—F. H. M., aged 36, a septipara in her eighth pregnancy, was admitted on March 7, 1940, two weeks before the expected date of confinement. She had been in labor for seven hours, and a fetal arm had been prolapsed for four hours; this may have prompted repeated examinations by a midwife. On admission, the abdomen was tender, and the fetal parts were easily felt. Decapitation was done, and the placenta was manually removed. On examination, complete rupture through the left wall of the lower uterine segment and the left broad ligament was found. Subtotal hysterectomy was done and followed by a blood transfusion. The postoperative course was uneventful, and the patient left the hospital after twenty days.

RUPTURE OF THE UTERUS DUE TO COMPOUND PRESENTATION OF THE FETUS

CASE 34.—K. K. T., aged 35, an octipara in her ninth pregnancy, was admitted on Oct. 30, 1937, three weeks after the expected date of confinement. She had been in labor with ruptured membranes for eight hours. There was slight contraction of the pelvis. On vaginal examination, it was found that both feet, the left hand and the head of the fetus presented at the pelvic inlet. Decapitation was done with difficulty, and thereafter an incomplete rupture in the anterior surface of the lower uterine segment was discovered. There were no external bleeding and no further interference. On the next day, the abdomen became distended, and the blood hemoglobin content dropped from 12.2 Gm. to 8.2 Gm. per hundred cubic centimeters. Blood transfusions were given, but the patient died.

CASE 35.—L. Y. Y., aged 31, a quintipara in her sixth pregnancy, was admitted on Nov. 30, 1938, four weeks before term. She had been in labor for twelve hours; the membranes had been ruptured for four hours, and she had been attended by a midwife. On admission, the patient was in a state of collapse, and there were no uterine contractions or fetal heart tones. On vaginal examination, the fetal head and arm were found presenting at the inlet, and there was a rupture extending through the lower uterine segment on the right side. An intravenous injection of dextrose solution was started, but the patient died ten minutes after admission.

RUPTURE OF THE UTERUS DUE TO EXCESSIVE SIZE OF THE BABY

CASE 36.—L. H. P., aged 32, a tertipara in her fourth pregnancy, was admitted on Jan. 23, 1938, one week past term. She had been in labor for sixty-six hours. During the last fourteen hours, the patient became short of breath; regular labor pains stopped, and the presenting part receded. On admission, the patient was in

a moribund state; the abdomen was tender; the fetal parts were easily felt, and no fetal heart tones were heard. When the abdomen was opened, the baby, which weighed 4,100 Gm., and the placenta were found in the peritoneal cavity. There was a rupture in the cervix extending into the anterior wall of the vagina. Total hysterectomy was done, and the patient died three hours after admission.

CASE 37.—C. C. J., aged 31, a tertipara in her sixth pregnancy, was admitted on July 24, 1937, twenty-six days after the expected date of confinement. She had been attended by a midwife during her labor of seventeen hours. The pelvic measurements were normal, and her previous deliveries had been uneventful. The patient was in good condition when admitted, and the cervix was completely dilated. The dead baby in breech presentation was extracted and was found to weigh 4,300 Gm. A rupture in the anterior surface of the lower uterine segment was found. At operation, the 12 cm. long transverse rupture was found completely to separate the bladder from the lower uterine segment. A blood transfusion was given, and subtotal hysterectomy was done. Five days after the operation, a vesicovaginal fistula was evident; this was repaired one month later. The patient was discharged twenty-six days after repair of the fistula.

CASE 38.—T. T. M., aged 21, a primipara in her second pregnancy, was admitted at term on Nov. 21, 1940, in a moribund condition. She had been in labor for seventeen hours, and the fetal arm had been prolapsed for eleven hours. Repeated manipulations by a midwife had caused much bleeding. The previous delivery had been uneventful. On admission, the patient was in a desperate condition. The abdomen was tender, and the fetal parts could be superficially felt. At operation, the peritoneal cavity was filled with old blood, the fetus and the placenta. The baby was dead and weighed 4,200 Gm. A complete rupture extended on the left from the cervix to the cornu. A blood transfusion was given, and subtotal hysterectomy was done. In spite of supportive measures, the patient died on the sixth day after operation. Autopsy demonstrated retroperitoneal abscess and general peritonitis.

RUPTURE OF THE UTERUS DUE TO HYDROCEPHALUS

CASE 39.—Y. J. C., aged 30, a sextipara in her seventh pregnancy, was admitted on Dec. 30, 1938, two weeks after the expected date of confinement. She had been in labor with ruptured membranes for eighteen hours; this resulted in delivery of the breech and body up to the shoulder girdle. A midwife had attended the case. On admission, the patient was in shock; the abdomen was tender and much distended, with shifting dulness, and the uterus was deviated to the right in a state of constant contraction. The presence of meningocele and hydrocephalus in the baby was clear, and delivery was readily effected by craniotomy. Examination thereafter showed complete rupture of the anterior wall of the lower uterine segment which extended into the left broad ligament. The patient promptly died.

CASE 40.—T. S. C., aged 23, a secundipara in her third pregnancy, was admitted on June 20, 1939, at term. She had been attended in her three day labor by a midwife. Regular labor pains had ceased sixteen hours prior to delivery. On admission, the patient was in coma; the temperature was 39.5 C. (103.1 F.), and the pulse rate was 160. The fetal heart could not be heard. A blood transfusion was given before the operation. At operation there was much free blood in the peritoneal cavity. The cervix and the uterus were completely torn through on the left side. The hydrocephalic fetus was still in utero. After extraction of the baby, subtotal hysterectomy was done. The patient died twelve hours after admission.

CASE 41.—C. T., aged 36, a sextipara in her seventh pregnancy, was admitted on Sept. 29, 1939, two weeks after the expected date of confinement. She was referred from another hospital after a labor of forty-four hours. Her pelvic measurements were normal, and all the previous deliveries had been uneventful. On admission, the patient was in shock; the fetal heart could not be heard, and the fetal parts were readily palpable. When the abdomen was opened, the fetus with hydrocephalus and meningocele was in brow presentation. A rupture of the anterior surface of the lower uterine segment extended into the fundus on both the right and the left side. Subtotal hysterectomy was done. A blood transfusion was given during the operation, and others were given repeatedly thereafter. A pelvic abscess developed; this was drained through the cervical stump. After a stormy course, the patient was discharged fifty days after the operation.

RUPTURE OF THE UTERUS DUE TO TUMOR OF THE FETUS

CASE 42.—C. P. H., aged 24, a secundipara in her third pregnancy, was admitted on Feb. 5, 1939, three weeks before the expected date of confinement. She had been in labor for sixteen hours, and the breech had protruded from the vulva for four hours. Attempts of a midwife to deliver the baby by traction had failed. A large tumor the size of a man's head over the sacral region of the baby was found to be the cause of the dystocia, and embryotomy was performed. Examination after delivery showed a tear into the left broad ligament. The abdomen became distended, and the patient ran a stormy course. On the twelfth postpartum day, the patient was reexamined, and a complete tear through the left broad ligament was found. The family insisted on taking the patient home, and attempts to follow up the case were unsuccessful. The tumor of the fetus proved to be teratoma.

RUPTURE OF THE UTERUS DUE TO THE PERSISTENT OCCIPITOPOSTERIOR POSITION OF THE FETAL HEAD

CASE 43.—C. C. T., aged 31, a quartipara in her fifth pregnancy, was admitted on June 26, 1940, and was said to be five weeks past term. She had been in labor for nineteen hours. A physician and a midwife had examined the patient and referred her to the Peiping Union Medical College Hospital. On admission, the fetal heart could not be heard, and the head presented deeply in the pelvis in left occipitoposterior position. The delivery was effected by means of craniotomy, cleidotomy and extraction. Vaginal examination then revealed rupture of the uterus. At operation, a tear was found in the anterior wall of the lower uterine segment under the bladder. This was repaired, and subtotal hysterectomy was done. Blood transfusions were given after operation and repeatedly during her stormy convalescence. The abdominal wound became infected, and secondary closure was necessary. The patient recovered and was discharged on the forty-fourth postoperative day.

RUPTURE OF THE UTERUS DURING PREGNANCY

CASE 44.—M. H. T., aged 39, a sextipara in her seventh pregnancy, was admitted on Nov. 12, 1938, at six months' gestation, because of sudden pain in the lower part of the abdomen accompanied by a fainting spell. She had been hospitalized in early pregnancy for hyperemesis. All previous deliveries had been uneventful. On admission, the patient was in a state of collapse. There was generalized abdominal tenderness and rigidity. The fetal heart was not heard, and there was no external bleeding. A transfusion of 500 cc. of blood was given before operation. On opening the abdomen, 3,000 cc. of dark blood was removed. The bleeding came

from a partial rupture of the posterior wall of the uterus near the right cornu. The dead fetus was removed by hysterotomy, and subtotal hysterectomy was done. Blood transfusions were given during the operation and repeatedly thereafter. The patient seemed on the way to recovery when symptoms suggesting thrombosis of the pelvic veins appeared. She died twenty-two days after the operation. The partial rupture was 4 cm. in length, extended 1 cm. into the myometrium and was caused by a ruptured varix.

DISTRIBUTION

Two of these patients were 19 years old, and the oldest was 43. Only 2 of the 44 patients were in their first pregnancy; this emphasizes the overwhelming incidence in multiparas. In 38 cases there were complete ruptures of the uterus, while in 6, the ruptures were incomplete. This

TABLE 1.—*Sites and Types of Rupture of the Uterus.*

Site	Type	
	Complete	Incomplete
Lower segment		
Transverse	13 (Cervix involved in 1)	
Left	11 (Cervix involved in 2)	3
Right	8 (Cervix involved in 4)	
Bilateral		2
Fundus		
Posterior wall		1
Anterior wall	2	
Bicornuate uterus	1	
Cesarean section scar	3	
Total	38	6

predominance of complete ruptures agrees with the findings of most authors on this subject, but we believe that incomplete rupture is much more common than is generally suspected. There must be many instances of postpartum bleeding caused by partial rupture in which the uterus is packed and the patient recovers without the cause of the bleeding being established.

As to location, in the group of complete ruptures, 11 were through the left lateral wall of the uterus; 8, through the right lateral wall; 13, transversely through the anterior wall; 3, through an old classic cesarean section scar, and 3, through the fundus. One of the last mentioned was through the horn of a bicornuate uterus (case 20). In the group of partial ruptures, 5 occurred in the lower uterine segment and 1 in the fundus. Of the ruptures in the lower uterine segment, 3 were found on the left side, and 2 were bilateral. Only 1 occurred during pregnancy, while 43 were associated with labor. Of the latter, 24 were judged to be due to maternal causes and 19 to be of fetal origin (table 1).

CAUSATION

Because so often many unknown factors were concerned, it is impossible accurately to classify these cases, but they have been grouped as to what seems to us to have been the primary etiologic factor. At this point, a few words concerning osteomalacia may be opportune. Osteomalacia is a progressive deficiency disease. Insufficient utilizable calcium and phosphorus in the diet with too little vitamin D together with a drain of these minerals such as occurs during lactation, may produce the condition. The common symptoms are aches and pains in the muscles and the bones of the thighs and the back. With sufficient decalcification, deformities of bone, especially of the pelvis and the spinal column, occur due to pressure. Pelvic deformity is characterized chiefly by varying degrees of collapse of the pelvis, marked shortening of the oblique diameters of the pelvic inlet and contraction of the transverse diameter of the outlet. In America, one seldom, if ever, sees deformity of the pelvis to such a marked extent.

With regard to the ruptures of the uterus thought to be due to maternal causes, in the first group caused by contraction of the pelvis, 9 out of 12 cases were due to osteomalacia. Two of the remaining 3 patients of this group, 1 of whom was a chondrodystrophic dwarf, had a generally contracted pelvis, and 1 had a simple flat pelvis. The efforts of a midwife to deliver the baby through insufficient space may have accounted for some of these ruptures. The remaining patients in this study all had pelvic measurements within the accepted limits of normal.

Rupture of the uterus through cesarean section scar occurred in 3 of these patients, 2 of whom had had infection of the abdominal incision after the previous operation. It is probable that these uterine scars were thin or poorly healed. Also, if the placental site is beneath the scar, the invasion of the chorion tends to weaken the wall of the uterus at this point, as emphasized by Holland.[3] The placental site was found beneath the scar in 3 of the 6 patients with rupture of a cesarean section scar observed in the Peiping Union Medical College Hospital, and this cause of rupture could be included as one of the intrinsic type mentioned by Seley.[4]

Trauma is known to have produced rupture of the uterus in 4 cases. The fumbling efforts of an untrained midwife to hasten delivery by pushing on the fundus of the uterus were responsible for the damage done in cases 16 and 18. The rupture in case 19 occurred in our own delivery room. We consider pushing on the uterine fundus instead of using forceps, where indicated, to be obsolete obstetrics even though it is still practiced by some. Kristeller's expression is no longer done in

3. Holland, E.: Proc. Roy. Soc. Med. (Sect. Obst. & Gynaec.) **14**:22, 1921.
4. Seley, A. D.: Am. J. Obst. & Gynec. **33**:857, 1937.

this hospital. Considering the history, the location and the type of rupture, it is probable that in case 17, the uterus was perforated during manual removal of the placenta.

Rupture through the pregnant horn of a bicornuate uterus at term is illustrated by case 20. An intrinsic cause, such as weakening of the wall of the uterine fundus associated with the congenital anomaly, is possible.

Four cases are included in our group of cases of rupture due to unknown causes. In 3 cases, the pelvic measurements were normal, and in 1, the mild degree of contraction of the transverse diameter of the pelvic outlet was probably not the cause of the rupture. All the babies were of normal weight. The ruptures in cases 21, 22 and 23 may have

TABLE 2.—*Classification of Cases According to Cause of Rupture of the Uterus.*

Cause	Cases	Outcome	
		Lived	Died
Rupture during labor due to a maternal cause:			
Contracted pelvis	12	4	8
Cesarean section scar	3	3	..
Trauma	4	3	1
Bicornuate uterus	1	1	..
Unknown cause	4	2	2
Rupture during labor due to a fetal cause:			
Transverse presentation	9	2	7
Compound presentation	2	..	2
Excessive size	3	1	2
Hydrocephalus	3	1	2
Tumor of the fetus	1	Unknown	..
Persistent occipitoposterior position	1	1	..
Rupture during pregnancy	1	..	1
Total	44	18	25

been due to the manipulations of the midwife in attendance, while in case 24, cervical dystocia or malposition of the fetal head may have caused the accident.

Turning to the baby as a probable cause of rupture of the uterus, one finds that there were 11 cases of transverse or shoulder presentation of the fetus. In 1 case, rupture was associated with a generally contracted pelvis (case 6), and in another, the baby was excessively large (case 38). These 2 cases are included in their proper groups. In 2 cases (cases 25 and 31), the rupture was probably caused by version and extraction before the patients were admitted here. The remaining 9 patients arrived at the hospital with neglected transverse presentation of the fetus. We have grouped them together under this heading, for it is impossible to estimate how much damage had been done by midwives trying to terminate labor by pulling on the fetal arm. It is possible also that our own careful efforts at decapitation may have in some instances completed the damage which was already started.

There were 2 instances of rupture due to compound presentation of the fetus; these were tragedies similar to some of those of the previous group. In case 34, decapitation may have contributed to the injury while patient 35 died within a few minutes after admission.

According to Lee,[5] in his review of 1,400 Chinese babies, the average weight is 3,000 Gm. We may consider that babies of more than 4,000 Gm. are definitely overweight. Since all 3 of our patients whose babies were listed as overweight had normal pelves, it is fair to assume that these ruptures of the uterus were caused by the excessive size of the baby.

In 3 cases, delivery was impossible because of hydrocephalus of the fetus. In case 39, it is probable that the rupture was caused by the traction with which the midwife tried to terminate the labor. Cases 40 and 41 were examples of injury to the patient because the attendant failed to recognize the condition.

The rare teratoma of the sacrum of the fetus was clearly the cause of the rupture of the uterus in case 42.

Persistent occipitoposterior position of the fetal head was responsible for only 1 of these accidents. The patient had had prolonged dry labor resulting in impaction of the fetal head. The signs and symptoms of rupture of the uterus were present on admission to the hospital, and it is not probable that a destructive operation on the fetus was the cause of the rupture.

Finally, there was only 1 case in which rupture was not associated with labor. This patient was in the sixth month of her pregnancy and had the typical symptoms of concealed hemorrhage. There had been no previous pelvic or abdominal operation, and the cause of rupture was established as a ruptured varix.

MORTALITY RATE AND PROGNOSIS

Eighteen of the 44 mothers lived; 25 died, and the outcome of 1 is unknown since she was discharged against the advice of the attending staff. Only 3 babies lived. In viewing this record one must consider the desperate condition of most of these patients when they arrived at the hospital. The length of labor is important because it influences the prognosis. Among those mothers who recovered, the average length of labor was seventeen hours compared with an average of thirty-eight hours for those who died. The time elapsing between rupture and treatment is also important. For those who recovered there was an average of six hours between the occurrence of the rupture and the treatment compared with an average of seventeen hours for those who

5. Lee, S. W.: Nat. M. J. China **14**:707, 1930.

died. The most frequent immediate causes of death were peritonitis, bronchopneumonia, bacteremia and paralytic ileus. It is surprising indeed that in 44 accidents attended by trauma to tissues and infection, thrombosis of the pelvc veins was suspected to have occurred only once. Phlebitis and thrombosis, however, are rare among the Chinese.

The widespread increase in the frequency of cesarean section makes the group of rupture of a cesarean section scar of especial importance. All 3 of the patients in this group recovered, and 2 of the babies lived. In a previous report from this department, Wang [2] described 3 cases of rupture of a previous cesarean section scar. Two of the patients lived, and 1 died of intestinal obstruction treated by enterostomy. All 3 babies died. The classic type of cesarean section had been done on all 6 of the patients with rupture of a cesarean section scar seen in this department. The conclusion from our experiences that in cases of rupture of a cesarean section scar, the mortality rate for mothers and babies is considerably less than in cases of other types of spontaneous rupture agrees with that of many authors on this subject. Rupture of the uterus is a gradual or sudden separation attended by much less bleeding, and the baby has more of an opportunity to act as a tampon in the uterine tear. Further, the patients who have had a previous cesarean section are on the lookout for trouble since they have been told, or should have been, that the next delivery should take place in a hospital. In the past year and a half, we have had 8 cases of rupture of the uterus, 7 of which were complete, with the loss of 2 mothers. Seven different members of the staff did these operations following rupture of the uterus. Subtotal hysterectomy was carried out on 7 patients, and on 1 occasion the tear was simply repaired. In all operations requiring removal of the uterus, the same general technic was used, and it seems to have been of value.

SIGNS AND SYMPTOMS OF THREATENED RUPTURE

During pregnancy there may be no premonitory signs of rupture. As long as the membranes are intact there is not much danger of this accident. An exception was case 44. Ruptures of the uterus with the membranes intact have been observed, but these are rare and are usually due to changes in the uterine wall rather than to retraction. When the membranes have ruptured and all fluid has been lost and good uterine contractions are present with no progress in labor, especially if the patient is a multipara, one should make a careful examination with a view of making an early diagnosis of the cause of dystocia. The uterus may be pulled farther and farther over the head or the body of the child, and the elastic cervix and lower uterine segment may be abnormally

stretched. The vaginal portion becomes clamped between the head and the pelvic inlet, and if this mechanism continues, rupture occurs. The signs of overstretching of the uterus in the presence of strong uterine contractions may be summarized as follows: (1) pain and tenderness over the lower part of the abdomen, with or without strong uterine contractions; (2) edema and change of color of that portion of the cervix which is clamped between the head and the pelvis; (3) a groove between the symphysis and the umbilicus or higher indicating the contraction ring; (4) tension of the round ligaments; (5) increase in the pulse rate.

TREATMENT OF THREATENED RUPTURE

The best treatment is, of course, prophylactic. Women who have had a previous cesarean section should be within easy reach of adequate surgical help during pregnancy and labor. The site of a previous cesarean section scar must be repeatedly examined during labor to detect excessive thinning or tenderness. One must not forget that in the patient who has undergone a previous classic cesarean section, one or more spontaneous deliveries thereafter weaken the uterus and predispose it to rupture rather than prove that the scar is strong. Separation of such a scar occurring late in pregnancy or in labor indicates the need for prompt surgical intervention. When, after a previous cesarean section, there has been infection and long convalescence, elective cesarean section should be considered. More rigid indications for the first cesarean section and less rigid indications for the second and common adoption of the low segment operation would considerably reduce the incidence of rupture of the uterus from this cause. If pituitary extract is used at all before delivery, not more than 3 minims (0.18 cc.) should be given at one time, and if the uterus reacts violently to such medication, small amounts of ether should be given to control the uterus until the effect of the drug is gone. The pituitary extract, however, was not a cause of rupture in this series. With the development of signs and symptoms of threatened rupture, immediate delivery is mandatory. Delivery with forceps may be contraindicated in these cases, and version and extraction are always contraindicated.

If the baby is dead, the problem in delivery from below is to reduce its size. Craniotomy and decapitation are the most useful procedures, depending on existing conditions. If the baby is living and the probabilities of infection are not too great, low cervical cesarean section gives the best prognosis for mother and child. If the baby is living and the uterus obviously infected, cesarean section followed by supravaginal amputation should be done.

SYMPTOMS AND SIGNS OF RUPTURE

At the time of rupture and thereafter, the signs and symptoms are definite. They vary somewhat according to whether the rupture is complete or incomplete. They may be summarized as follows:

1. Sudden sharp pain, followed by the symptoms of shock, is present (33 cases).

2. There is gradual cessation of uterine contractions, which may indicate incomplete rupture (5 cases), or sudden cessation of strong contractions, which indicates complete rupture (21 cases).

3. There are changes in the contour of the abdomen. The baby may be more easily palpable (19 cases), and a tumor mass representing the uterus may be felt in either lower quadrant of the abdomen.

4. Bleeding depends on the extent of the tear. When the signs of hemorrhage are out of proportion to the amount of visible bleeding, one should think of concealed hemorrhage. Acute anemia gradually develops. Thirteen of our patients had acute anemia, but many were so dehydrated with consequent concentration of hemoglobin that the actual number of cases of anemia is not known.

5. A slowly growing tumor alongside of the uterus, with developing emphysema and bleeding, is indicative of incomplete rupture (case 12).

6. Recession of the presenting part before delivery may occur (3 cases). Retention of the placenta after delivery has been seen occasionally.

TREATMENT AFTER RUPTURE

After every difficult delivery, especially when associated with manipulation or instrumentation, the physician should explore the uterus and the lower part of the genital tract. If incomplete rupture is found, repair from below and packing can frequently be carried out. Even when the rupture is complete, one may be forced to rely on packing as the only available method of treatment. Two cases of this sort were reported by Maxwell [6]; both patients lived. According to Freund,[7] the mortality rate after packing of the uterus in instances of complete rupture is about twice as great as when treatment by supravaginal amputation of the uterus has been carried out. However, even in a case of incomplete rupture of the uterus, if a hematoma is already present alongside of the uterus, abdominal operation should be carried out when the patient is in a condition to withstand the procedure. If complete rupture is found, one should prepare to give a transfusion, and while waiting for blood, one should give adequate dextrose, usually from 500 to 700 cc.

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6. Maxwell, J. P.: China M. J. **24**:341, 1910.

7. Freund, R., in Halban, J., and Seitz, L.: Biologie und Pathologie des Weibes, Berlin, Urban & Schwarzenberg, 1927, vol. 8, pt. 1, p. 863.

of a 20 per cent solution; this should be given slowly after testing the urine for sugar. The infusion requires about one hour. The dextrose infusion should be replaced by blood as soon as this is available. When the child is free in the abdominal cavity, attempts to deliver it through the tear are absolutely contraindicated; this was emphasized by De Lee,[8] but the procedure is still, unfortunately, occasionally done.

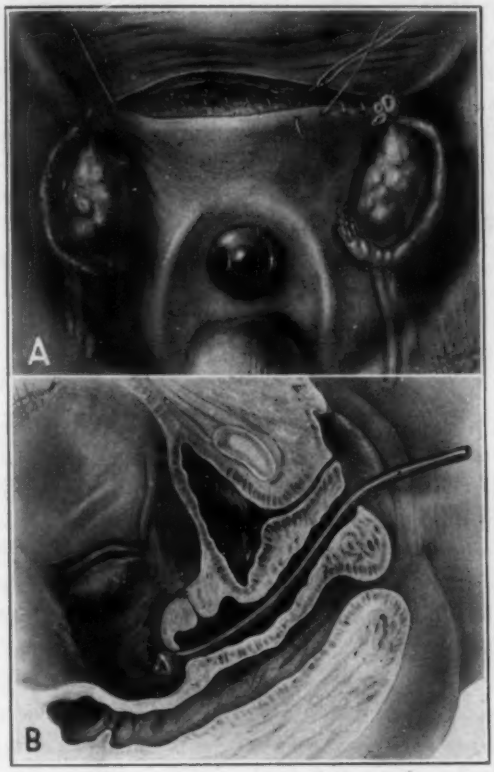
Packing from below is sometimes useful to control bleeding while preparations for operation are in progress. Sometimes rupture at the site of a previous cesarean section scar can be treated by excision of the scar and repair, but in other cases, when the tear is uneven, removal of the uterus by supravaginal hysterectomy is the treatment of choice, because such a procedure controls the bleeding and removes the focus of infection. Most patients are in such a critical condition that a prolonged operation is undesirable.

Our results have considerably improved with the adoption of a simple technic. In some instances, the cervix was found to be torn, and the rupture extended up through one broad ligament. Removal of the cervix is not urgent, and we usually prefer not to extend the operation by removing it. We believe that as nearly uniform a technic as possible is the answer to the problem as regards the surgical treatment of this condition in any hospital. The technic must not be complicated, so that any one familiar with abdominal operations can do it. The surgical procedure at this hospital is a modification and a combination of the technic observed in several hospitals and may be briefly described as follows:

The position of the patient on the operating table is important in order that the operator can do his best work. We have removed the foot or lower one third of the table for all gynecologic laparotomies. The patient's thighs are placed in leg holders on the same level as the abdomen; the knees are widely separated, and the buttocks protrude slightly beyond the edge of the table, while the legs simply hang at the knees. The operator and his first assistant are alone on each side of the table and are not encumbered by the presence of too many persons in close quarters. The second assistant stands between the patient's thighs and close-up in the field. After the abdomen is opened and the fetus and the placenta are removed, the bladder fold of the peritoneum is first transversely incised and pushed downward with the bladder. This transverse incision is continued into the tear in the damaged broad ligament. If a hematoma is present, it can be quickly evacuated and the bleeding points controlled. The second assistant is in position to help identify disturbed anatomic relations. With the gloved hand, from

8. De Lee, J. B.: Principles and Practice of Obstetrics, ed. 7, Philadelphia, W. B. Saunders Company, 1938, p. 860.

below if necessary, he can readily identify the torn cervix and the vaginal vault for the operator. By the use of through and through sutures, the rent in the cervix can be quickly and safely repaired, and the uterus may then be amputated as in any supravaginal hysterectomy. A continuous suture is placed in the remaining cervical portion (*A* in the illustration), which begins laterally at one angle and includes the mucosa and about one half of the thickness of the musculature across the cervix



In *A* is shown how, after supravaginal amputation of the uterus, the remaining cervical portion is closed with a continuous suture in two layers. This is simple and prevents oozing. In *B* is shown how, after closure of the cervix, insertion of a large mushroom catheter through the posterior vaginal vault into the cul-de-sac provides easy, quick and efficient drainage.

to the opposite angle. The same suture may be continued back to its original point, including the remaining muscle wall and serosal surface. Oozing is thereby prevented. The ligamentous attachments of the uterus are loosely anchored to the angles of the cervix with the same continuous suture, and the bladder fold of peritoneum is used to cover the raw surface. Drainage through the cul-de-sac by means of a

large mushroom catheter is easily provided (*B* in the illustration). The second assistant is in position to place an open clamp in the posterior vaginal vault beneath the posterior lip of the cervix, and the cul-de-sac is incised from above in order to place a drainage tube into the vagina. We believe that such a procedure provides better drainage than through the cervix or the abdominal wall. Ruptures which do not involve the cervix and its attachments are simpler to handle. The prevention and the treatment of ileus in the early postoperative period by decompression of the gastrointestinal tract by means of continuous suction have been of great value to these frankly infected patients. During this procedure, it is important to provide adequate amounts of physiologic solution of sodium chloride and dextrose solution, usually by the intravenous drip method. Uniformity in procedure is essential in any hospital if good results are to be obtained. The adoption of this technic, the liberal use of blood transfusions and parenteral fluids, the prevention of distention of the stomach and the upper part of the bowel by the application of continuous suction and the judicious use of chemotherapy have materially improved our results. After the initial blood transfusion subsequent transfusions are usually necessary, depending on the degree of anemia of the patient.

SUMMARY

The details about 44 patients with rupture of the uterus treated in the Peiping Union Medical College Hospital during the past seven years have been reviewed. Year by year there has been a definite decrease in the mortality rate. The reasons for this decrease are: (1) improvement in the availability of blood for transfusion; (2) the adoption of a uniform technic in the surgical treatment; (3) the use of sulfanilamide and its derivatives; (4) the decompression of the gastrointestinal tract by the use of continuous suction.

In the treatment of acute anemia nothing takes the place of blood, and the convenience of using stored blood is of obvious importance. Improvements in chemotherapy have been a decided help to our patients and have no doubt prevented deaths in the late postoperative period, since most of those who died succumbed soon after operation and before the drug had had an opportunity to take effect. Although modifications must be made to meet the problems of individual cases, we believe that it is worth while to note the advantages of uniformity in the surgical procedure. We have therefore described the method in use at this hospital. It is true that the incidence of rupture of the uterus indicates the character of obstetric practice in any community, and further reduction in the present mortality rate must depend on better obstetric practice. This will come when the public understands the dangers of childbirth and when training programs for midwives and physicians gradually take effect.

TREATMENT OF BURNS OF THERMAL ORIGIN

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During the past three years the literature on the treatment of burns has been prolific. Most of the articles have dealt with some one phase of the subject. Blood studies in shock due to burns and the correction of blood imbalance have come in for particular emphasis.

This communication is intended to be more comprehensive. It stresses again the improvement in the mortality rate due to the use of plasma in the treatment of shock accompanying severe burns. In addition, it undertakes to discuss other important factors concerned in the clinical management from the time of the accident to eventual cure or death. The article comprises two comparative series, one of 188 cases encountered from 1930 to 1939, the other of 92 cases occurring from March 1939 to November 1941. The reason underlying the comparison is that the latter series has been under the uniform management of a burn service in contradistinction to an unregulated regimen in the previous decade.

To facilitate the discussion, the factors concerned may be listed chronologically under the following heads: (1) the treatment of shock; (2) local cleansing of the burned area; (3) treatment of the burned area with various agents; (4) the removal of the eschar (if escharotic agents are used) and epithelization with or without graft; (5) complications; (6) prevention of contractures and follow-up with or without plastic reconstruction.

SHOCK

"The period of shock in a burned patient is an entity itself and should be treated as such." [1] "We should fix attention upon the measures which affect the survival of the patient, regardless of their influence upon infection or epidermal growth." [2]

Despite these warnings, physicians when first called and interns in receiving wards are still at times so taken with the pitiful state of the patient that their attention is directed to the treatment of the burned

From the Department of Surgery, University Hospital.

1. Aldrich, R. H.: Role of Infection in Burns, New England J. Med. **208**: 299-309, 1933.

2. Glover, D. M.: A Critical Evaluation of the Treatment of Burns, Ann. Surg. **113**:1090-1091, 1941.

area instead of to the treatment of shock. By this error, valuable time is lost, and this is responsible for death, especially of infants and young children.

For a severe burn seen by a physician at the patient's home the treatment is clear. The patient should be wrapped in sheets, blankets or any available covering, receive an injection of morphine and be removed as quickly as possible to an institution, where adequate shock treatment can be given. The treatment of the burned area is of secondary importance until shock has been treated and the patient is responding. This response may not be evident for several hours; during this period the lesions remain covered.

Much valuable contributory work has been done since 1920 and especially since 1930 to illustrate the conception of shock due to burns. Among the outstanding contributors have been Underhill,[3] Davidson,[4] Blalock,[5] Scudder,[6] Moon,[7] Elkinton,[8] Harkins,[9] Dunphy,[10] Freeman,[11] Davis[12] and many others, whose voluminous work cannot be reviewed in this article.

There are still controversial points as to the mechanism of the production of shock. There is, however, abundant experimental and clinical evidence to show that after a severe burn there is altered capillary permeability at the site of the burn with a leakage of the fluid portion of the blood at the site. In addition to the external loss there is also a greater accumulation of fluid in the tissues.[8] This loss of fluid results

3. Underhill, F. P.; Kapsinow, R., and Fish, M. E.: Studies on Mechanism of Water Exchange Induced by Superficial Burns, Am. J. Physiol. **95**:315-339, 1930.

4. Davidson, E. C.: Tannic Acid in the Treatment of Burns, Surg., Gynec. & Obst. **41**:202-221, 1925.

5. Blalock, A., and Mason, M. F.: Blood and Blood Substitutes in the Treatment and Prevention of Shock, with Particular Reference to Their Use in Wartime, Ann. Surg. **113**:657-671, 1941.

6. Scudder, J.: Shock: Blood Studies as a Guide to Therapy, Philadelphia, J. B. Lippincott Company, 1940.

7. Moon, V. H.: Shock: Its Mechanism and Pathology, Arch. Path. **24**: 642-663 (Nov.); 794-810 (Dec.) 1937.

8. Elkinton, J. R.; Wolff, W. A., and Lee, W. A.: Plasma Transfusion in the Treatment of the Fluid Shift in Severe Burns, Ann. Surg. **112**:150-156, 1940.

9. Harkins, H. N.: Experimental Burns: I. The Rate of Fluid Shift and Its Relation to the Onset of Shock in Severe Burns, Arch. Surg. **31**:71-85 (July) 1935.

10. Dunphy, J. E.: Observation of the Pathology of Experimental Traumatic Shock, Surg., Gynec. & Obst. **72**:823-833, 1941.

11. Freeman, N. E.: The Mechanism and Management of Surgical Shock, Pennsylvania M. J. **42**:1449-1452, 1939.

12. Davis, H. A.: The Pathology of Shock in Man, Arch. Surg. **41**:123-146 (July) 1940.

in decrease of blood volume, blood flow (cardiac output) and plasma protein with accompanying hemoconcentration. These alterations can be well illustrated by various blood studies which constitute the basis for the use of intravenous plasma. Elkinton estimated that this shift or leakage continues until the fortieth hour after trauma, but in some of the cases in this series, blood balance was not obtained for fifty to sixty hours.

Recently Rhoads [13] reported that supplementing plasma with extract of adrenal cortex reduces the leakage period to as low as eighteen hours after shock. He warned that sodium chloride should be given only as indicated by blood estimations, as extract of adrenal cortex causes marked chloride retention.

Management of Shock.—In the clinical management of shock, it is the practice to obtain a basal line blood chemistry as quickly as possible after the usual shock measures have been instituted. Blood for this purpose is taken at the time plasma is first given (usually 500 to 1,000 cc. for adults, less for children). In hospitals in which blood banks are operating, this treatment can be started twenty to thirty minutes after the arrival of the patient. Requisitions on the first blood sample are made for hematocrit, red blood cell, hemoglobin and plasma protein determinations which are repeated at six hour intervals. These determinations are used as indexes for the amounts and the frequency of later plasma administration. Determinations of carbon dioxide, nonprotein nitrogen and chlorides are made on later blood samples. The giving of small amounts (300 to 500 cc.) of plasma every four to six hours, depending on the severity of shock as indicated by the hematocrit and protein studies, is advised. Recently, Harkins [14] reported a simple way to estimate the dose of plasma needed. "The amount of plasma needed can be roughly calculated for an average-sized adult as being 100 cc. plasma for every point the hematocrit exceeds the normal of 45, as long as the plasma proteins are above 6.0 Gm. per hundred cubic centimeters. When the plasma proteins are below 6.0 Gm. per hundred cubic centimeters, an additional 25 per cent of the calculated amount of plasma should be added for every gram the protein is below 6.0." An attempt is made to keep the protein at 6 mg. per hundred cubic centimeters and the hematocrit at 50 to 55 during the period of leakage.

At this institution, each unit (500 cc.) of plasma may be defined as the fluid portion obtained from 500 cc. of whole citrated blood, which is diluted to 1 pint with physiologic solution of sodium chloride.

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13. Rhoads, J. E.; Wolff, W. A., and Lee, W. A.: The Use of Adrenal Cortical Extract in the Treatment of Traumatic Shock of Burns, Ann. Surg. **113**:955-965, 1941.

14. Harkins, H. N.: Personal communication to the author.

Intravenous dextrose and sodium chloride are contraindicated during this period of shock since they will increase the tissue edema already present. Crystalloid solutions are rapidly lost from the circulation in a shocked patient and actually wash plasma protein out of the blood stream.[15] Plasma given frequently in indicated amounts is the answer to correcting protein loss until the period of leakage has stopped. In burns involving 30 to 40 per cent of the body area, the total amount of plasma necessary is approximately 4,000 cc. in the average adult. Then, any remaining protein deficiency can be readily corrected by using whole blood.

The handling of such a patient necessitates a hospital with an operating blood bank, day and night laboratory facilities and constant attention from the house and visiting staffs. By constant care in the first several days of the shock period, lives can be spared.

It is not intended to convey the impression that every patient shocked from burns can be saved by the present improved methods. At a certain level shock becomes an irreversible process. It is, however, to be emphasized that treatment of shock in cases of severe burns is of the greatest importance. It is not common sense in the light of present knowledge to spend the first valuable hours in cleaning and treating burned areas with local agents, only to lose the patient from shock. The importance of constant vigilance to this ever present complication of severe burns cannot be too often reiterated. Especially is this so in the case of children who are so labile in this regard and who, according to McClure,[16] make up 45 per cent of the 8,000 persons with lethal burns per year in this country.

LOCAL CLEANSING OF THE BURNED AREA

After the work and teachings of Davidson,[4] McClure,[16] Mason,[17] Aldrich [18] and others there should be no controversy about cleaning a burned area.

A burn should be considered as an open contaminated wound consisting for the most part of dead or damaged tissue. There should be no more hesitancy about cleaning a burned area than about cleaning a

15. Harkins, H. N.: The Treatment of Burns, Brochure Prepared in Connection with Exhibit on Burn Shock, Scientific Exhibit, Section on Surgery, Ninety-Second Annual Session of the American Medical Association, Cleveland, June 2-6, 1941. Blalock and Mason.[5]

16. McClure, R. D.: The Treatment of the Patient with Severe Burns, J. A. M. A. **113**:1808-1812 (Nov. 11) 1939.

17. Mason, M.: Local Treatment of the Burned Area, Surg., Gynec. & Obst. **72**:250-253, 1941.

18. Aldrich, R. H.: Preoperative and Postoperative Treatment, Philadelphia. W. B. Saunders Company, 1937, pp. 256-287.

compound fracture or a laceration. The surgical principle is the same, though the specific methods are different.

Although the burned area may be sterile immediately after the accident, it is usually contaminated before the patient reaches the hospital. Most burns fall heir to some salve or grease. It is a great help to receive the patient with a sheet, towel or blanket over the burn instead of a greasy dressing which takes time to remove. This procedure of cleansing is essential in the successful treatment of burns regardless of the agent subsequently to be used.

Method of Cleaning.—After shock treatment has been instituted and the patient is responding, the cleaning of the burned area is begun. The patient should be removed to a suitable room for this purpose. There, under aseptic precautions—gloves, mask, cap, gown—the area should be cleaned as quickly, thoroughly and gently as possible. A scrubbed team of two or three will expedite the procedure. Depending on the foreign substance present, e. g., tar, grease and clothing, the areas are cleansed with soap, water or ether, with soft gauze or cotton pledgets. After thorough cleaning and removal of gross debris, the blisters are opened, and the redundant skin is removed.

The employment of anesthesia in cleaning depends on individual preference and the condition of the patient. Anesthesia has been employed in selected cases for some patients of this series, especially for excited unruly children. Light pentothal sodium is the anesthetic of choice. For adults, morphine and barbiturates have proved adequate in most cases. As Aldrich [1] pointed out, ether applied directly to the burned area does not hurt as much as one might suppose. The area of the burn is estimated and charted after the method of Berkow.[19]

TREATMENT OF THE BURNED AREA WITH VARIOUS AGENTS

Since records have been available, literally hundreds of different agents have been advised. The history of the treatment of burns by the ancients and others through the nineteenth century would in itself make an interesting narrative. Thus, it is not the purpose of this paper to favor any particular agent or to give credit to any single method, since splendid results are being obtained at different clinics with various agents. As a caution to those who may read without question of the claims made for various agents, it is well to remember that it is difficult if not impossible to make a satisfactory comparison between groups of cases in which the degree of shock, the degree of the burn and the area involved may differ so widely. Regardless of the agent employed,

19. Berkow, S. G.: A Method of Estimating the Extensiveness of Lesions (Burns and Scalds) Based on Surface Area Proportions, Arch. Surg. **8**:138-148 (Jan., pt. 1) 1924.

destroyed tissue must be replaced by scar or graft, and no agent will do this. The purpose of any agent is to serve as a protective and an antiseptic scaffolding under which epithelial proliferation may take place.

Today agents for treatment can be generally classified under salves, ointments, pastes and jellies and eschar-producing and noneschar-producing solutions. For severe burns, eschar-producing solutions are more widely used. However, some clinics use sterile petrolatum or ointments, even for major burns. Of all agents used, tannic acid preparations in

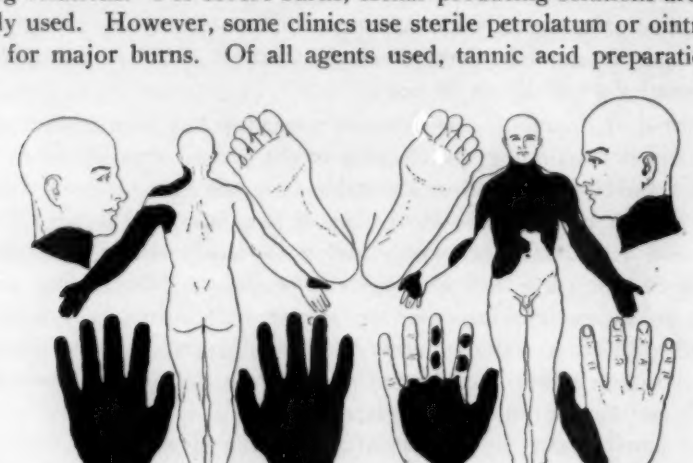

Fig. 1.—Reproduction of a printed form used to record blood studies and the area burned, using the Berkow estimations of skin surface.

Lower extremities (including buttocks)	38 per cent	Foot (one sixth of lower extremity)	3 per cent
Trunk (including neck)	38 per cent	Lower leg (one third of lower extremity)	6-7 per cent
Upper extremities	18 per cent	Thigh (one half of lower extremity)	9-10 per cent
Head	6 per cent	Total area burned	40 per cent
Hand (one fourth of an upper extremity)	2-3 per cent	Combined 2d and 3d degree	40 per cent

A. S. White man 48 Gasoline Admitted: 6-2-41 Discharged: 11-5-41

	6-2-41 12:05 a. m.	4 a. m.	4 p. m.	6-3-41 8 a.m.	6-4-41 8 p. m.
Hematocrit	52	49	48	47	40
Hemoglobin	128	112	106	104	84
Red blood cell count	5.40	6.02	5.21	.....	4.080
Protein	8.7	7.11	.....	5.26	6.1
Nonprotein nitrogen	55	36	.....	39	30

Treatment: 6-2-41 Plasma 2,500 cc.—total 4,000 cc. fluids by mouth and infusion
6-3-41 Plasma 900 cc.—total 1,200 cc. fluids by mouth and infusion
6-4-41 Plasma 500 cc.—total 3,100 cc. fluids by mouth and infusion

By blood culture: 6- 7-41 Bacillus coli } Both septicemias
6-17-41 Staphylococcus haemolyticus } responded to chemotherapy

Operations: Five stages of skin grafting; also amputation of left hand.

various percentages and forms are undoubtedly the most popular. Chief among eschar producers are tannic acid alone [4] or tannic acid followed by silver nitrate,[20] gentian violet, the triple dye mixture [18] and lately sulfadiazine (2 - [paraaminobenzenesulfonamido] - pyrimidine) spray. Many agents are available, each with its particular advantages and disadvantages. However, one surgical principle is essential to remember, that only a sterile nonirritating preparation should be applied to a surgically cleaned burned area.

Method of Treatment.—Burns at this clinic are not consistently treated with eschar-producing agents, but when their use is elected, the triple dye mixture of Dr. Robert Aldrich of Boston is employed. The dye mixture consists of gentian violet, brilliant green and acriflavine. The dye was chosen because it has a high specificity against gram-positive and gram-negative organisms as well as the ability to form, if properly applied, a thin pliable eschar.

The mixture does not deteriorate over a long period of time. In comparison with tannic acid, it is more expensive and more soiling, and the eschar takes longer to dry. On the other hand, the dye is more antiseptic and forms a thinner and more pliable eschar, under which infection is easier to detect. The dye can readily be removed from the person of the nurses or the operators with aromatic spirit of ammonia.

The technic employed is much like that of tannic acid application. After thorough gentle cleansing of the involved areas, the dye mixture is applied by sterile cotton pledgets six to eight times at twenty minute intervals. The patient is then transferred to a sterile bed. A cradle is placed over the bed, and heat slightly above 40 C. is maintained by electric bulbs. The drying of the eschar at times takes as long as twelve to eighteen hours, and every effort is made to keep the patient from contamination during this period. The pain is relieved after the first or second coating as with any other agent. The resultant eschar is deep purplish black with a gold-green sheen.

After the application of the dye, the treatment calls for constant vigilance. The proper diet and administration of fluids are maintained. Frequent inspection of the burned areas and recordings of the pulse rate and the temperature are essential, as well as frequent blood examinations. In ideal cases, if a small area of the back, the chest, the abdomen or an extremity is involved, sterility is usually easy to maintain. Unfortunately, however, these cases are infrequent. Burns around certain body orifices make infection inevitable, but the infection can be detected in the eschar, usually within twenty-four to forty-eight hours. The eschar becomes soft and moist, loses its sheen and changes to a

20. Bettman, A. G.: Tannic Acid and Silver Nitrate in Burns, Surg., Gynec. & Obst. **62**:458-463, 1936.

lighter blue. It can be removed with little difficulty. The infected area may be soaked with warm saline compresses for twenty-four to forty-eight hours and the dye reapplied without sacrificing the entire eschar.

An especial note of caution is directed to those who employ tanning agents—these solutions should never be used on the eyelids, the fingers, the hands or the toes. Ectropion is a common sequel. Venous and lymphatic obstruction by compression of vessels between an eschar and close underlying bone results in chronic dactylitis and deformity. After the usual cleansing, the fingers, the face and the toes are treated with gauze impregnated with bismuth tribromphenate. The digits are carefully covered separately so that burned surfaces are not in apposition. They are dressed only once every seventy-two hours unless they become infected. In this event, sterile saline compresses are used; these are removed down to the tissue every four hours until the infection has abated.

In burns about the face, the eyes should be examined thoroughly as soon as possible lest they close by edema. Regardless of the presence or absence of scleral or corneal injuries, the pupils are dilated with several drops of 1 per cent atropine. If injury is present, consultation is requested. Patients must be assured that they are not blind but that the lids are swollen shut. The edema usually persists seven to ten days before the lids function properly. During this time no attempt is made to pry open the lids for instillations. As the edema subsides, the conjunctivas are irrigated if necessary. Due to the orbicularis reflex, the eyes are not as a rule seriously injured.

REMOVAL OF THE ESCHAR AND EPITHELIZATION WITH OR WITHOUT GRAFT

There is no arbitrary day set for the removal of the eschar. The removal depends on the degree of the burn and the state of the eschar, i. e., whether infected or not.

If the burn is mainly second degree with only scattered small areas of greater depth and the crust has not become infected, the eschar is allowed to remain until complete healing has taken place. If it is allowed to remain, the eschar may begin to loosen and curl at the margins eight to fifteen days after the application of the agent. At this time, perhaps only ¼ to ½ inch (0.6 to 1.3 cm.) of the border may become loose. If this occurs, the loose border is removed with sterile scissors and forceps, and the underlying new tissue is painted with a 5 per cent aqueous solution of gentian violet. At other times when the margin of the eschar loosens a considerable area (10 by 15 cm.), it may be removed and the underlying tissue may be found to be covered with

a layer of yellow fatty-looking material. The material may be mistaken for pus, which it is not. The material is plasma that has escaped after the agent was applied and has become concentrated under the eschar. It must be remembered that patients are treated for burns after they respond to shock therapy but not necessarily after they are cured of the shock. So, at times, leakage of body fluid continues after application

Fig. 2.—W. G., aged 18 months, was scalded by water. *A*, appearance of the eschar ten days after the burn. *B*, appearance after removal of the eschar eighteen days after the burn. *C*, appearance on the day of discharge, thirty-two days from the time of admission.

of the eschar. This, too, is thought to be the reason for the wrinkled, ballotable eschars that sometimes occur, and they should not be removed simply because pus is suspected as the cause for their elevation unless there are other indications. This yellow material can be easily removed in twenty-four hours by compresses, after which some stimulating gauze

impregnated with bismuth tribromphenate or ointment of scarlet red is applied for several days until healing is complete.

If the burn is predominantly third degree, the eschar is electively removed from the fifth to seventh day after application of the dye with the patient under anesthesia. This time is chosen in order to allow the

Fig. 3.—A. S., aged 48 years, was burned by gasoline on June 2, 1941. *A*, appearance of the eschar four days later. The eschar was removed eleven days after the accident. The underlying tissue was treated with warm saline compresses for five days and then grafted. *B*, photograph taken fifteen days after grafting. *C*, photograph taken thirty-five days after grafting.

patient to recover from shock. The eschar is removed aseptically in the operating room. Sterile bandages are applied snugly for one night. The following day they are soaked thoroughly with sterile solution of

sodium chloride and removed. Compresses are then applied regularly until the tissue is suitable for grafting, usually within two to four days. The importance of early grafting in third degree burns cannot be overemphasized.

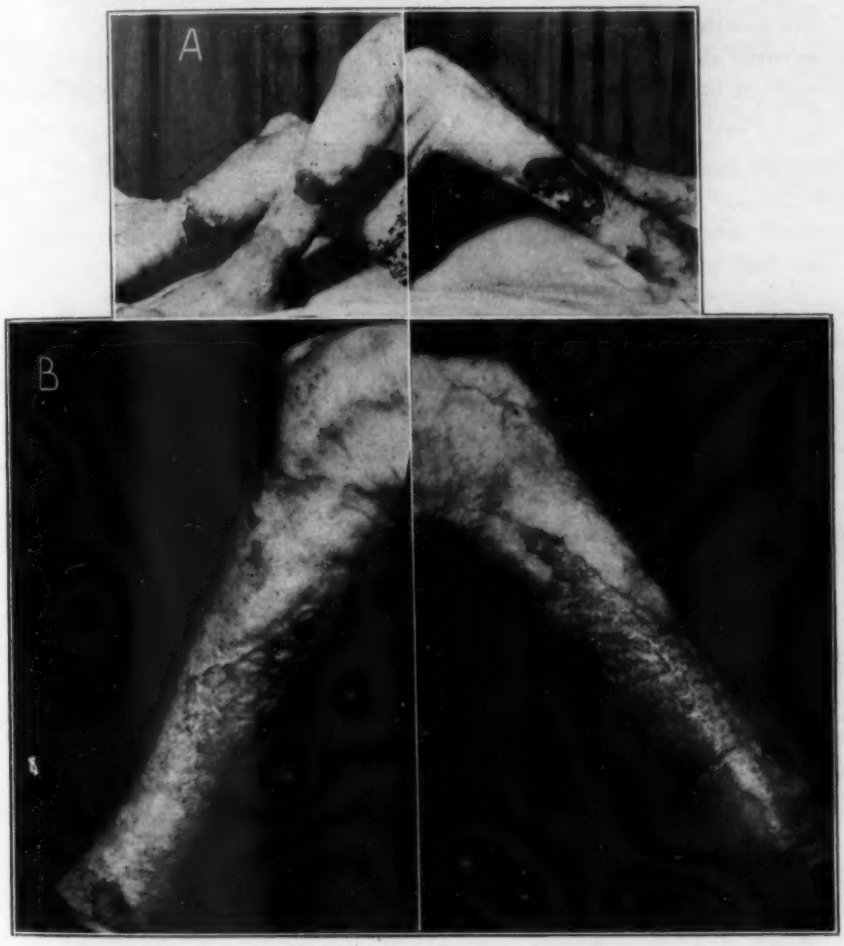

Fig. 4.—W. M., aged 31 years, was burned by gasoline six years before admission. *A*, indolent ulcers at the time of admission. *B*, end result nine months later.

If the eschar in second or third degree burns becomes infected, it should be removed and the underlying area treated with compresses until granulation appears suitable for grafting. If the area is large, grafting may be performed in several stages; in these cases, the Davis or small deep graft is usually employed. Between stages, exuberant

granulations are controlled with copper sulfate crystals or a saturated solution of copper sulfate, which is less damaging to epithelial buds than silver nitrate. Ordinary alcoholic antiseptics are not employed because they retard the healing process. Only aqueous preparations are used.

A severe burn under ideal circumstances may necessitate three to five months' hospitalization—much longer if grafting is delayed. Large wounds allowed to granulate may heal after months of daily dressings, only to break down again at the slightest strain on the new inelastic

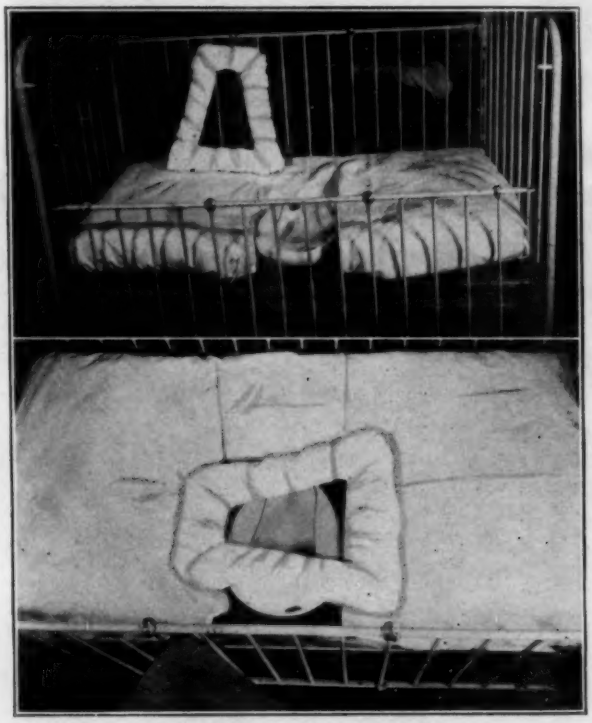

Fig. 5.—Two views of the crib, the mattress, the padded splint and the bedpan used in treating infants and young children with burns of the posterior surfaces of the body and the extremities.

scar. This is especially true of the lower extremity, where dependent mechanical elephantiasis develops in addition to indolent recurrent ulceration. These disabling complications can be forestalled by early grafting. Late grafting may even produce good functional results but under less favorable circumstances.

The stage between removal or peeling of the eschar and final healing is little discussed; this is justifiable, since patients rarely follow a regular

charted course. This stage can be fraught with many complications, such as resistant secondary anemia, septicemia, pneumonia, local coccogenous infection, indolent granulations, pyocyaneus infection and psychoses. Ideally, a patient with a second degree burn might be discharged cured in twenty-one days; but if complications ensue, death may occur, or healing may be prolonged for weeks. Only those who follow the cases day by day can appreciate this long and at times discouraging stage of treatment.

COMPLICATIONS

There are three theories as to the so-called toxic phase accompanying severe burns: (1) the physical theory, in which the toxic course is thought to be due to fluid imbalance; (2) the old specific toxic theory of absorbed foreign protein, exploded by Underhill [3]; (3) the bacterial theory, which supports infection as the only cause. This question is a mooted one and will not be reviewed in this paper, but in my observations, I have never seen a septic course in the absence of infection.

Anemia.—Anemia of the secondary type is specifically noted because of its constant presence in severely burned patients and because of the necessity of its correction to induce healing. Anemia becomes more troublesome after the eschar is removed and large granulating areas are exposed. Before, after and between stages of grafting, continuous attention must be paid to the blood picture. This is especially true of children. A complete blood picture should be made at least once a week, and treatment of the anemia should be made by oral medication or transfusion. Grafting should not be performed on a patient with a hemoglobin value under 75 per cent. As much care should be given to maintain blood levels and vitamin concentration in patients with burns as in any other patients hospitalized for long periods.

Septicemia.—Septicemia is always a lurking danger when large areas of tissue are exposed to infection. It may occur either early in spite of meticulous cleansing or late between stages of eschar removal and grafting. Again, it may occur when eschars become infected. Any sudden rise in temperature with or without chill should indicate the immediate withdrawal of blood for culture. One patient in the present series had positive blood cultures on two occasions in a six week period—colon bacillus on the first and Staphylococcus haemolyticus on the second occasion, both times responding to chemotherapy. Another patient had a blood culture positive for infection with Bacillus pyocyaneus from which he succumbed on the thirty-ninth day of the burn. The early recognition of this complication and treatment with chemotherapy will save lives.

Pneumonia.—Pneumonia complicating a burn is a serious and often fatal disease. Anoxia, fluid imbalance and pain, with shock, together with drugs administered for their relief may so retard respiration as to encourage early atelectasis and bronchopneumonia. Pneumonia may be an early or late complication. In children particularly, it runs a rapid and fatal course in spite of oxygen and chemotherapy. In this series, 4 of the 12 deaths were due to pneumonia. Of the 4 patients, all were under 4 years of age.

Persistent Coccogenous Infection.—Persistent coccogenous infection with resulting indolent granulations, more prevalent in older patients, can usually be traced to some general systemic cause. In cases in which heavily infected granulations do not progress normally, the red blood cell count and the hemoglobin and the protein content should be thoroughly examined; vitamin intake estimations and dietary studies should be checked. If the general condition is found satisfactory, attention is directed to the local tissue. With the patient under anesthesia, the tissue and the surrounding skin are painted with tincture of iodine. In addition, the granulations are painted with one application of saturated silver nitrate and then excised with a scalpel. Hot saline compresses are applied until bleeding is controlled, and ether is poured over the denuded area to aid drying and cleansing. The area is grafted at the same sitting. In some instances, this procedure will promote epithelization promptly. In other instances it must be repeated.

Pyocyaneus Infection.—Infection by B. pyocyaneus of the areas during epithelization has been a frequent complication in ward cases. It can quickly be eliminated by applying gauze dressing saturated with 3 per cent acetic acid to the area for twelve hours. This will eradicate the organism for indefinite periods and can be reapplied in case of reinfection. This treatment will not kill or hinder the growth of grafts.

Urinary Suppression.—Urinary suppression is most frequently seen in older patients during the first several days of the shock stage. In this series it has not been common. The treatment consists of giving concentrated dextrose intravenously and solution of sodium chloride by infusion if possible. The urine should be examined at least twice a week, even in the absence of urinary suppression, especially when wound infection is present. When the triple dye mixture is used as the therapeutic agent, false positive bile urine reactions may be present for some days owing to the absorption of the brilliant green from the mixture.

Fever.—Fever that is persistent in burned patients can usually be traced to infection. It is not unusual to find small infected lesions (10 by 5 cm.) that produce temperatures of 101 to 103 F. Constant daily inspection is necessary to eliminate this annoying indication of general systemic reaction. However, if the examination is thorough, an infected area can usually be found within twenty-four hours.

Mental Reactions.—The mental reactions of burned patients should not be ignored. Fear of pain and disfigurement are the patient's chief source of concern. Protracted hospitalization may be the cause of depression and melancholia, even to the point of desire for death. As soon as the condition of the patients will permit, a frank discussion of the condition is held. If the patient's mentality permits, the course of treatment is roughly outlined. It is not wise to underestimate the time necessary for cure. An occasional word of encouragement is helpful. Sources of physical irritation should be minimized. Dressing should be performed slowly and painstakingly and, if possible, by the same doctor on every occasion. Anesthesia should be employed in the removal of eschars, and compresses, when used, should be warm, not hot. The morale of the patient is dependent to a marked degree on the kindness, gentleness and prudent care of the physician.

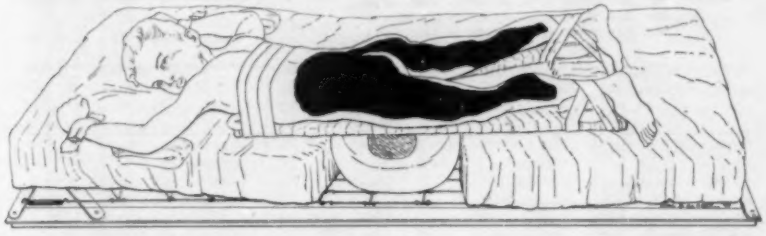

Fig. 6.—Illustration of the method of restraint and the use of the splint and the special mattress in treating burns of the posterior aspect of the body in infants and young children.

PREVENTION OF CONTRACTURES AND FOLLOW-UP WITH OR WITHOUT PLASTIC RECONSTRUCTION

Suspicious contracture areas are considered immediately after the burn has been treated. When possible, splints or other devices are used to prevent or minimize the resultant scar. It is not always possible, however, to use splints or casts because of circumferential burns which need frequent dressings. In such cases, the prime consideration is epithelization of the area and plastic reconstruction later. Measures for contracture prevention may tax the physician's ingenuity to the utmost. In infants and young children the spread eagle splint has been found to be of great aid in treating burns of the back, the buttocks and the posterior portions of the lower extremity. This splint of basswood is cut to individual pattern, well padded and strapped to the child. The child is then placed face down on a basal metabolism mattress. From the first, the removable portion of the mattress is withdrawn, and a bed pan is inserted to catch the excreta. At intervals of five to seven days, the splint is changed. Some patients are treated in this manner until complete healing has taken place.

On discharge, the patient is instructed in the care of the new epithelium. Daily massage with castor oil is of aid to prevent drying, scaling and itching. Bland nonirritating soaps should be used. Care should be exercised in exposing the new covering to sun, wind and cold. At this clinic, where burns are assigned to the surgical service, the responsibility remains with that service until the burn is epithelized,

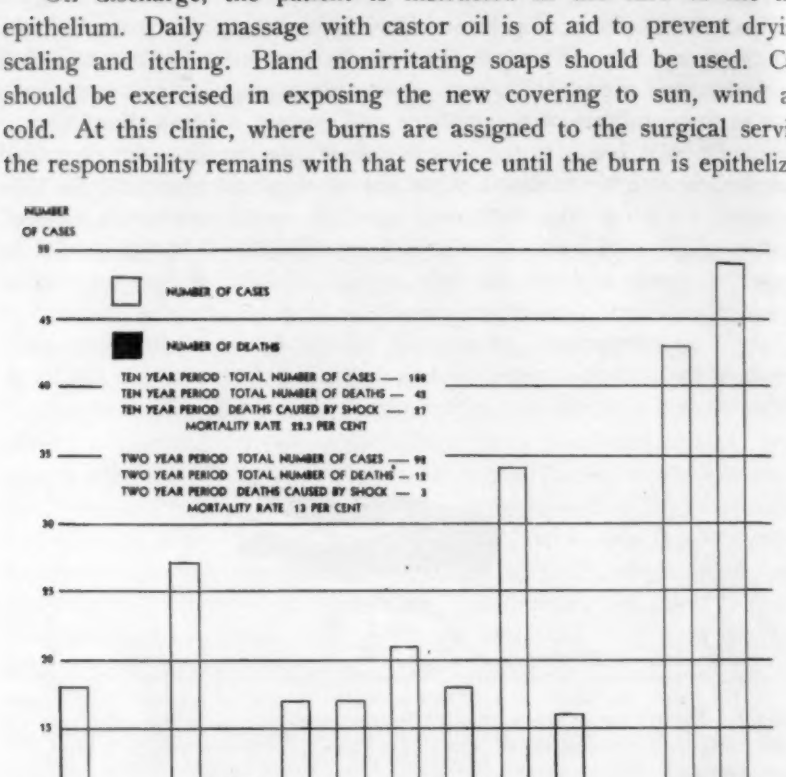

Fig. 7.—Graph showing the number of patients with burns admitted and the number who died from burns at the University Hospital in the past twelve years.

which may include grafting. Procedures of reconstruction or release of contractures are assigned to the department of plastic surgery. Patients are instructed to report for examination semiannually, especially children, in whom contraction may develop with growth.

STATISTICAL REVIEW

The review of cases includes the admissions in the period from March 1939 to November 1941; these comprise 92 patients.

Patients with burns make up only 0.014 per cent of the total admissions to the general surgical service. Of the 92 patients, 63 were male and 29 female. The industrial patients were all males. Seventy-five were white, and 17 were Negroes.

It is of economic interest to note that of the 92 patients, 56 were charity; 32 were compensation, and 4 were private. The age range was from 14 months to 64 years. All of the industrial patients were over 21 years of age. Of the 56 free patients, 35 were children of 10 years or under.

The causative agents were either scalding water or flames (from house fire, bonfire, gasoline, oil, gunpowder or gaseous explosions).

Mortality Statistics

Case	Age of Patient	Cause of Burn	Area Involved, per Cent	Time of Death After Accident	Autopsy	Agent Used	Cause of Death *
1	22 mo.	Boiling water	45	23 days	....	Escharotic	Bronchopneumonia
2	3½ yr.	Boiling water	25	46 days	....	Escharotic	Bronchopneumonia
3	25 yr.	Flame (gasoline)	40	5 days	Yes	Escharotic	Pulmonary edema
4	47 yr.	Flame (gasoline)	48	33 days	....	Escharotic	Pyocyaneus septicemia
5	6 yr.	Flame (gas stove)	57	11 days	Yes	Escharotic	Pulmonary edema
6	50 yr.	Flame (oil stove)	90	3 days	Yes	Escharotic	Shock
7	3 yr.	Flame (gas stove)	27	25 days	....	Escharotic	Bronchopneumonia
8	64 yr.	Flame (house fire)	48	12 hrs.	....	Escharotic	Anesthetic
9	5 yr.	Flame (oil)	50	4 hrs.	Yes	Ointment	Shock
10	4 yr.	Flame (house fire)	15	10 days	....	Escharotic	Bronchopneumonia
11	20 mo.	Boiling water	65	2½ hrs.	....	Escharotic	Shock
12	3 yr.	Flame (gasoline)	68	10 days	....	Escharotic	Intravenous sodium bicarbonate to combat acidosis

* Summary of deaths: The causes were: pulmonary complication in 6 cases; shock in 3; septicemia in 1; anesthetic in 1, and intravenous reaction in 1. Three cases are open to criticism. Anesthesia should never have been used in case 8. This was poor judgment; the patient never reacted from the anesthetic. In case 11 there was a bad error in judgment. The child was not treated for shock before the treatment of the burn was considered. In case 12, death occurred six hours after the intravenous use of sodium bicarbonate in treating acidosis, and no other cause was found for the death.

No chemical or electric burns were included in this series. The time spent in the hospital varied from fifteen days to six months. The body area involved varied from 12 to 90 per cent by Berkow's standard of estimation. Of the 92 patients, grafting was done on 17. The number of graftings varied from one to five stages on the same patient. The small deep graft of Davis was used in all cases; in addition Thiersch grafts were used in 2 patients.

Mortality Figures.—In the decade 1930 to 1939 at the University Hospital there were treated 188 thermal burns with 42 deaths—a mortality rate of 22.3 per cent. In the past twenty-one months there were treated 92 patients with 12 deaths—a mortality rate of 13 per cent.

It is interesting to note that in the 42 deaths of the previous decade, 27 occurred within the first seventy-two hours from shock, while in the

present series only 3 died from shock. Had these 27 patients lived through the shock period there might conceivably have been a mortality rate of only 8 per cent. These figures would then show that shock therapy with the use of plasma has lowered the mortality rate but that the treatment of burns or burn complications has improved but little. Of the 12 deaths in the last series, 8 or 75 per cent occurred in children 6 years of age or under.

SUMMARY AND CONCLUSIONS

Three surgical principles are emphasized in the treatment of burns: (1) the primary treatment of shock before considering treatment of the burned area; (2) the recognition of a burn as an open contaminated wound, which should be properly cleaned before treatment; (3) the choosing of a sterile and nonirritating agent for the treatment of the burned area.

Patients with severe burns when first seen should be given morphine, should be wrapped with some covering (no greasy preparation should be applied to the burn) and should be sent as rapidly as possible to a hospital where proper shock therapy can be given.

Plasma therapy in the treatment of shock due to burns has, as in this series, definitely lowered the mortality rate. Infants and children are particularly labile as regards shock and should be treated for it whether or not they exhibit clinical signs. Though the reported mortality rate of 13 per cent is in no way remarkable, deaths from shock have dropped to 3 among the last 92 patients treated compared with 27 among the previous 188.

Cleansing of a burn should not be undertaken until the patient is responding well to shock therapy. Cleansing should be done under aseptic conditions as quickly, gently and thoroughly as possible.

Eschar-producing agents are preferred at this clinic for the treatment of burns involving multiple areas. They should not, however, be used on the fingers, the hands, the toes, the feet or the face. Agents do not replace destroyed tissue, and after their use the patient must be watched daily for all complications that can develop in the stage between the accident and the cure. Pneumonia complicating burns in infants and children has proved rapidly fatal in spite of modern therapy.

Patients with third degree burns can be spared many weeks in the hospital by skin grafting performed as soon as the condition of the patient permits.

It is a prediction that hospitalization for patients with burns will be prolonged in the future, because some of the severely burned patients who died from shock in the past will now be saved owing to improved methods in shock control.

HEPATIC FUNCTION AND THE FORMATION OF HIPPURIC ACID

RESPONSE TO THE ADMINISTRATION OF AMINOACETIC ACID AND SODIUM BENZOATE IN PATIENTS WITH SUBNORMAL CAPACITY FOR SYNTHESIS

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In Quick's hippuric acid test, the benzoic acid administered as sodium benzoate brings two mechanisms into action in the liver: (1) the production of aminoacetic acid and (2) the conjugation of aminoacetic acid with benzoic acid to form hippuric acid. Quick[1] stated that the diminution of hippuric acid formation in patients is due mainly to the reduced ability of the liver to synthesize aminoacetic acid and in part to damage of the enzymatic mechanism performing the conjugation. This suggests that patients with diminished hepatic ability to furnish aminoacetic acid should respond with an increase in excretion of hippuric acid if aminoacetic acid is administered along with sodium benzoate. On the other hand, patients in whom the conjugation process also is impaired should not show such an increase.

METHOD

To probe the validity of this assumption, we decided to determine the hippuric acid formation in patients to whom sodium benzoate was given with and without aminoacetic acid. Haines, Magath and Power,[2] studying patients with hyperthyroidism, performed this experiment on 8 of their subjects. They stated that their results were not consistent and proposed to study this problem further. In a previous article,[3] we reported the results of such an experiment in 5 normal subjects and in 6 patients with low excretion of hippuric acid. In the present

This study was aided by the Louis M. Monheimer Research Fund.

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1. Quick, A. J.: Clinical Value of the Test for Hippuric Acid in Cases of Disease of the Liver, Arch. Int. Med. **57**:544 (March) 1936.

2. Haines, S. F.; Magath, T. B., and Power, M. H.: The Hippuric Acid Test in Hyperthyroidism, Tr. Am. A. Study Goiter, 1939, p. 277.

3. Probstein, J. G., and Londe, S.: Studies of Liver Function by Means of Quick's Hippuric Acid Test, Ann. Surg. **111**:230, 1940.

study we made observations on 24 additional patients whose excretion of hippuric acid was below normal. While the test was run for four hours on all of these patients, it was carried out for only one hour on the normal subjects in the studies previously reported. For purposes of adequate comparison, it was therefore necessary to perform the full four hour test on a few more normal subjects. The standard dose of 4 Gm. of sodium benzoate was used for the first test, while a mixture of 5 Gm. of aminoacetic acid and 4 Gm. of sodium benzoate was used for the second.

RESULTS

As shown in table 1 and chart 1, the addition of aminoacetic acid caused a marked rise in the hippuric acid excreted during the first hour by 4 normal subjects; they were all able to eliminate 39 per cent or more of the ingested sodium benzoate in one hour. The character of the curve of the hourly rate of excretion also was changed, in that

TABLE 1.—*Effect of Ingestion of Aminoacetic Acid on Synthesis of Hippuric Acid in Normal Subjects*

		Percentage of Sodium Benzoate Excreted				
Subject	With or Without Aminoacetic Acid	First Hour	Second Hour	Third Hour	Fourth Hour	Total
1	Without	28	34	25	7	94
	With	45	37	7	0	89
2	Without	25	34	28	5	92
	With	42	27	0	0	69
3	Without	23	33	25	10	91
	With	40	35	7	0	82
4	Without	25	31	28	9	93
	With	39	27	6	0	72

the peak of hippuric acid synthesis appeared during the first hour, while it appeared during the second hour when sodium benzoate alone was taken. Interestingly enough, subject 2 eliminated no hippuric acid during the last two hours of his second test. Thus, despite the markedly increased output of hippuric acid during the first hour, this subject excreted only 69 per cent in four hours, as compared with 92 per cent when he took sodium benzoate alone. Subject 4 showed practically the same picture; he eliminated only 72 per cent in four hours after taking the aminoacetic acid–sodium benzoate mixture, as compared with 93 per cent after taking sodium benzoate alone.

These two observations, plus the fact that a number of patients to be discussed later behaved in a similar fashion, stimulated our interest in the possible reasons for this phenomenon. As one possibility, it may be assumed that while a part of the aminoacetic acid was used for conjugation with benzoic acid, another part was catabolized. The remaining free portion of the benzoic acid, then, may have been insufficient to

stimulate the liver to furnish a new supply of aminoacetic acid. However, we found that in 1 of our normal subjects a small dose of sodium benzoate (1 Gm.) exerted enough stimulus to enable him to eliminate 65 per cent of it in one hour.

Another possibility to be considered is that the aminoacetic acid–producing stimulus of the remaining benzoic acid may be inhibited by the deaminizing process which is set in motion by the ingested aminoacetic acid and which, gaining momentum, continues after deamination is complete. We, therefore, in a series of experiments on 1 of the normal subjects, administered 1 Gm. of sodium benzoate at varying intervals after the ingestion of 5 Gm. of aminoacetic acid to provide benzoic acid

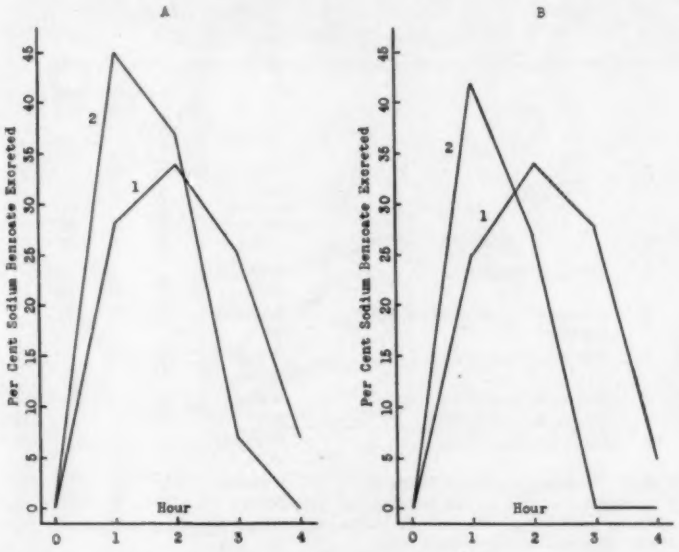

Chart 1.—Two types of response to the addition of aminoacetic acid in normal subjects. *A*, subject 1 (table 1): *1*, after sodium benzoate; *2*, after aminoacetic acid–sodium benzoate mixture. *B*, subject 2 (table 1): *1*, after sodium benzoate; *2*, after aminoacetic acid–sodium benzoate mixture.

in the blood during and after deamination. However, at no time were we able to demonstrate a suppression of hippuric acid synthesis.

Still another factor which we have not investigated should be mentioned. In 1931, Quick [4] and, recently, Wagreich, Abrams and Harrow [5]

4. Quick, A. J.: The Conjugation of Benzoic Acid in Man, J. Biol. Chem. **92**:65, 1931.

5. Wagreich, H.; Abrams, A., and Harrow, B.: Detoxification of Benzoic Acid by Glucuronic Acid in Humans: Rate of Detoxification, Proc. Soc. Exper. Biol. & Med. **45**:46, 1940.

showed that in human subjects definite portions of ingested benzoic acid are excreted in conjugation with glycuronic acid. There is the possibility that the latter mechanism may be stimulated in some by ingesting aminoacetic acid and sodium benzoate, with the result that two reactions compete for the benzoic acid and the aminoacetic acid loses the contest.

Of the 30 patients studied, 5 (patients 1 to 5 in table 2 and chart 2) whose initial excretion of hippuric acid was low were unable to respond with an increased rate of hippuric acid synthesis after the administration of the aminoacetic acid–sodium benzoate mixture. A sixth patient

TABLE 2.—*Patients with Impaired Ability to Synthesize Hippuric Acid Who Did Not Respond with an Increase in Hippuric Acid Synthesis to the Ingestion of Aminoacetic Acid*

Patient	Age, Yr.	Sex	Diagnosis	With or Without Aminoacetic Acid	Percentage of Sodium Benzoate Excreted				
					First Hour	Second Hour	Third Hour	Fourth Hour	Total
1	55	M	Portal cirrhosis	Without	7	14	14	14	49
				With	3	23	16	8	50
2	46	M	Common duct obstruction; jaundice	Without	13	29	23	9	74
				With	16	22	28	3	69
3	63	F	Portal cirrhosis	Without	..	5*	4	4	13
				With	10	0	0	0	10
4	37	M	Diabetes; probable polycystic kidney; enlarged liver	Without	13	15	8	12	48
				With	18	15	9	10	52
5	48	M	Small liver; jaundice	Without	11	14	22	16	63
				With	10	14	20	..	44†
6	56	M	Duodenal ulcer with fistula of bile duct into the duodenum	Without	15	28	11	26	82
				With	15	32	26	7	80

* Excreted in this and the preceding hour.
† Total for three hours only.

(patient 6, table 2), a borderline subject, showed an abnormal lag in the first two hours of his original test but excreted 82 per cent, a normal amount, in four hours. Adding aminoacetic acid did not overcome the lag, there being no increased response during the first two hours of the second test. Thus, in this patient, as in the first 5 mentioned, there was a defect in the conjugation process. This defect and a diminished ability of the liver to furnish aminoacetic acid were probably both responsible in patients 1 to 5, while in patient 6 only the conjugating mechanism was damaged, since the lag was not overcome by the addition of aminoacetic acid.

The remaining 24 patients all showed a rise in the rate of hippuric acid synthesis during the first two hours of the test with added amino-

acetic acid (table 3), but when we examined their excretion of hippuric acid during the entire four hour period, we found different types of response.

One type, represented by the largest group (patients 1 to 12), was like that of normal (or at least borderline) subjects when tested with sodium benzoate only. The patients were enabled by aminoacetic acid to eliminate 50 per cent or more of the ingested sodium benzoate (the excretion of only 1 remaining a little below this limit) in the first two hours. Ten patients in this group excreted 78 per cent or more in the four hour period. (The lower limit of normal with sodium benzoate alone is 80 per cent.) In every case the quantity of hippuric acid excreted during the first two hours and during the entire four hour period was

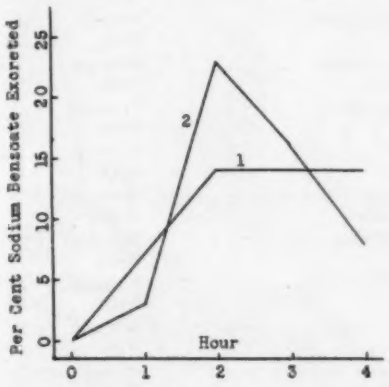

Chart 2.—Lack of response to the addition of aminoacetic acid in patient 1 (table 2) with impaired ability to synthesize hippuric acid: *1*, after sodium benzoate; *2*, after aminoacetic acid–sodium benzoate mixture.

definitely greater than when the patient was tested with sodium benzoate only (chart 3 *A*).

The second type (shown by patients 13 to 20, chart 3 *B*) was also the excretion of over 50 per cent of the ingested sodium benzoate during the first two hours when aminoacetic acid was given, but with considerable diminution of hippuric acid synthesis after this period. As a result, in 6 of these cases, the quantity of hippuric acid eliminated in four hours was no greater, and in some was even less, than when sodium benzoate alone was given. In the remaining 2 cases there was an increase in the four hour total, but not nearly so great as that seen in patients 1 to 12. Since the same kind of lag was observed in normal subjects, we cannot consider these patients to be more severely affected than those responding with a markedly increased four hour total.

TABLE 3.—*Patients with Impaired Ability to Synthesize Hippuric Acid Who Responded with an Increase in Hippuric Acid Synthesis to the Ingestion of Aminoacetic Acid*

Patient	Age, Yr.	Sex	Diagnosis	With or Without Aminoacetic Acid	Percentage of Sodium Benzoate Excreted				
					First Hour	Second Hour	Third Hour	Fourth Hour	Total
1	50	M	Stricture of common duct, postoperative, still jaundiced	Without	17	20	22	6	65
				With	30	45	12	4	91
2	50	F	Stenosis of common duct; jaundice	Without	12	12	13	10	47
				With	27	32	20	6	85
3	32	F	Cholelithiasis	Without	12	20	21	10	63
				With	37	12	30	0	79
4	75	F	Subsiding cholelithiasis and acute cholecystitis	Without	6	28	11	0	45
				With	18	31	16	6	71
5	31	F	Cholelithiasis, obesity	Without	16	23	22	14	75
				With	38	34	9	0	81
6	20	M	Catarrhal jaundice	Without	11	15	19	15	60
				With	21	36	18	3	78
7	23	F	Hyperthyroidism	Without	..	15*	15	21	51
				With	26	43	..	14*	83
8	25	F	Hyperthyroidism	Without	..	10*	0	1	11
				With	38	42	5	0	85
9	56	M	Asthma	Without	20	31	16	7	74
				With	18	45	16	6	85
10	27	F	Paroxysmal hypertension; adrenal tumor (?)	Without	7	21	26	3	57
				With	16	44	17	1	78
11	81	M	Severe sunburn	Without	4	13	16	16	49
				With	24	20	16	15	75
12	49	F	Proliferative arthritis	Without	15	12	15	22	64
				With	45	36	7	3	91
13	38	F	Hemolytic icterus; splenectomy	Without	19	18	22	6	65
				With	28	35	4	0	67
14	46	F	Early hepatic cirrhosis; large liver and spleen	Without	11	21	8	7	47
				With	35	31	1	0	67
15	56	M	Cholelithiasis; bile duct obstruction; jaundice	Without	13	0	34	18	65
				With	19	44	4	2	69
16	58	F	Cholelithiasis; bile duct obstruction; jaundice	Without	15	14	20	0	49
				With	28	29	3	4	63
17	30	F	Hyperthyroidism	Without	19	26	17	5	67
				With	37	14	4	1	56
18	36	M	Hodgkin's disease	Without	24	34	13	2	73
				With	34	30	8	2	74
19	41	M	Advanced dementia paralytica, tabetic form	Without	17	14	19	16	66
				With	14	44	6	1	65
20	46	M	Chronic peptic ulcer	Without	15	22	28	7	72
				With	20	40	9	0	69
21	40	M	Arsphenamine hepatitis; jaundice	Without	4	13	9	22	48
				With	12	35	17	5	69
22	28	F	Exfoliative dermatitis	Without	17	17	18	14	66
				With	15	33	9	11	68
23	45	F	Carcinoma of the liver	Without	2	13	10	17	42
				With	3	29	15	9	56
24	70	M	Paget's disease; carcinoma of colon	Without	7	11	9	12	39
				With	17	8	33	14	72

* Excreted in this and preceding hour.

The last 4 patients also showed a rise in the rate of hippuric acid synthesis but could not attain a 50 per cent elimination during the first two hours. The excretion during the entire four hour period also remained at a low level.

CONCLUSIONS

Normal adults taking 5 Gm. of aminoacetic acid and 4 Gm. of sodium benzoate eliminated more than 39 per cent of the sodium benzoate during the first hour after ingestion of the mixture. This rate of hippuric acid synthesis was much higher than that in the same normal subjects when they ingested 4 Gm. of sodium benzoate only. A marked drop in the

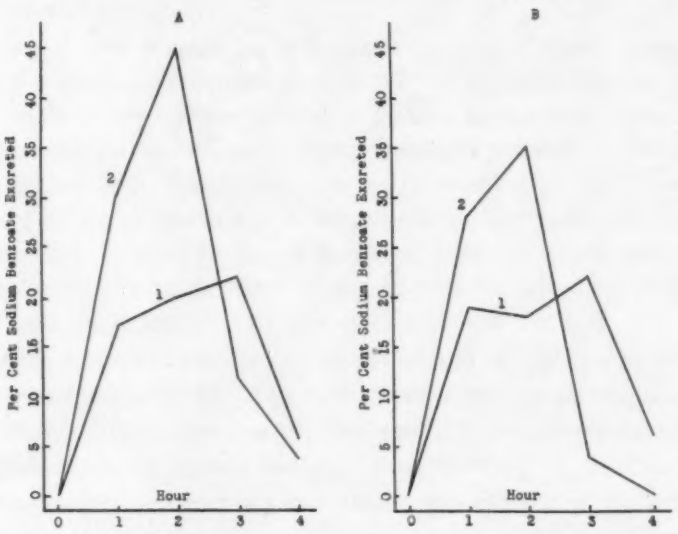

Chart 3.—Two types of increased response to the addition of aminoacetic acid in patients with impaired ability to synthesize hippuric acid. *A*, patient 1 (table 3): *1*, after sodium benzoate; *2*, after aminoacetic acid–sodium benzoate mixture. *B*, patient 13 (table 3): *1*, after sodium benzoate; *2*, after aminoacetic acid–sodium benzoate mixture.

excretion of hippuric acid occurred in the last two hours of the test in 2 of the normal subjects, so that the total amount eliminated in four hours was considerably less than that excreted when sodium benzoate alone was taken.

Six of 30 patients with impaired ability to synthesize hippuric acid showed no increase in the rate of synthesis when aminoacetic acid in addition to sodium benzoate was administered to them. Thus, definite impairment of the conjugation process was demonstrated in these patients.

The other 24 patients responded with a rise in the rate of hippuric acid synthesis during the first two hours. In these patients, it is concluded, the decreased elimination of hippuric acid during the standard four hour test was due mainly to a diminished ability of the liver to furnish aminoacetic acid.

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PROTHROMBIN TEST AS A DIAGNOSTIC AND PROGNOSTIC AID

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During the past five years much has been written about vitamin K, and in many previous publications the causes of hypoprothrombinemia have been reiterated.[1]

It is not the purpose of this paper to review those causes but rather to present additional evidence to support the belief that the results of the prothrombin test are helpful in making an accurate diagnosis in the jaundiced patient. Also, in many instances a rough estimation of the extent of liver dysfunction can be determined. In addition, the results of the prothrombin test in 36 patients with intestinal dysfunction are presented to give further support to previous conclusions[2] that hypoprothrombinemia develops owing to lack of adequate food, loss of bile from the intestinal tract or a combination of the two.

The prothrombin test was carried out on 120 patients, most of whom had hypoprothrombinemia. The method employed was the one described by Quick,[3] and each time the test was used the thromboplastin solution was checked against normal plasma. Four to 8 mg. of 2-methyl-1, 4-naphthoquinone[4] (vitamin K) was usually given orally in divided doses over twelve to eighteen hours to patients for whom treatment was desirable. It is believed that it is better to give a large dose so that

From the Department of Surgery, University Hospitals of Cleveland.

1. (*a*) Butt, H. R.; Snell, A. M., and Osterberg, A. E.: The Preoperative and Postoperative Administration of Vitamin K to Patients Having Jaundice, J. A. M. A. **113**:383-389 (July 29) 1939. (*b*) Quick, A. J.: The Clinical Significance of Prothrombin as a Factor in Hemorrhage, Pennsylvania M. J. **43**:125-130 (Nov.) 1939. (*c*) Abbott, W. E., and Holden, W. D.: Hypoprothrombinemia in Intestinal Disorders, Am. J. Surg. **53**:215-218 (Aug.) 1941.

2. Clark, R. L., Jr.; Dixon, C. F.; Butt, H. R., and Snell, A. M.: Deficiency of Prothrombin Associated with Various Intestinal Disorders, Proc. Staff Meet., Mayo Clin. **14**:407-416 (June 28) 1939. Abbott and Holden.[1c]

3. Quick, A. J.: The Nature of Bleeding in Jaundice, J. A. M. A. **110**:1658-1662 (May 14) 1938.

4. Supplied by Eli Lilly & Co., Indianapolis.

the maximal response to the therapy can be determined in twenty-four to forty-eight hours. When patients were thought to have insufficient bile in the intestinal tract, 0.32 Gm. of bile salts [4] was administered with each 2 to 4 mg. of vitamin K.

The various types of cases are separated into groups for the sake of clarity.

LEUKEMIA

Five cases of leukemia were studied in which the initial prothrombin levels varied between 62 and 82 per cent. The average was 76 per cent of normal. Two of the patients were seen several years later and showed prothrombin amounts about 10 per cent below the former levels. Shortly afterward, both patients died, and autopsy revealed hepatomegaly with leukemic infiltration. Vitamin K therapy failed to produce any change in the prothrombin levels of these patients.

LAENNEC'S CIRRHOSIS

Twelve patients with Laennec's cirrhosis were studied; in most of these the condition was moderately far advanced. The initial prothrombin values ranged between 40 and 86 per cent of normal with an average value of 61 per cent. Many of these patients received vitamin K in adequate amounts and failed to show any response. The dose was then increased, and bile salts were administered, but still no response was obtained. In a patient who had a prothrombin level of 40 per cent, there was a gradual lowering to 25 per cent in a week, even though he received vitamin K. During this time, the icteric index was rising to 90, and the blood urea nitrogen was increasing. He died of hepatic insufficiency. In 3 cases, it was thought that exploration to rule out obstructive jaundice was indicated. The icteric indexes in these patients were 90, 131 and 140. The prothrombin tests revealed levels below normal, and the patients failed to respond to extensive therapy over three to six day periods. Because of this, it was believed that cirrhosis was present. Operation confirmed this impression in each instance. The bile ducts were patent and normal in size.

TUMOR OBSTRUCTING THE BILE DUCTS

There were 9 cases in which there was a tumor obstructing the bile ducts (table 1). In these, the prothrombin levels varied between 0 and 83 per cent. The average level was 43 per cent of normal. The 3 patients (table 1) with levels of 0, 10 and 21 per cent were bleeding when they entered the hospital. The first 2 responded well to therapy

with vitamin K and bile salts. This response was characteristic of almost the entire group. Patient 4 was admitted to the hospital for terminal care because of carcinomatosis with obstruction of the common duct due to extrinsic pressure. At the time of admission, the prothrombin level was 90 per cent of normal, and during the two ensuing weeks, it gradually fell to 31 per cent. After 2 mg. of 2-methyl-1, 4-naphthoquinone and 1.28 Gm. of bile salts were given, the prothrombin level returned to 96 per cent in twenty-four hours. It remained there or slightly above for three days without further therapy, and then during the next week fell to 70 per cent, at which time the patient died.

TABLE 1.—*Cases of Tumor Obstructing the Bile Ducts*

	Prothrombin Level, Percentage of Normal					Treatment		
Case	Initial	After Vitamin K	Final	Highest Icteric Index	Hours Between Tests *	Vitamin K, Mg.	Bile Salts, Gm.	Comment
1	0	100	...	115	24	8	2.56	Bleeding from gums, bladder and gastrointestinal tract stopped with vitamin K
2	10	100	70	120	48	14	5.12	Hematuria stopped with vitamin K
3	21	...	...	130	..	0	0	Because of age and condition no therapy
4	31	96	70	120	24	16	1.28	
5	54	100	80	115	24	4	0.64	
6	60	92	100	45	14	6†	0	
7	64	50	50	43	48	8	1.28	Autopsy revealed hepatomegaly (4,500 Gm.) with biliary cirrhosis and metastasis
8	68	100	...	100	24	5†	....	
9	83	...	...	100	..	..	....	

* Hours between initial prothrombin test and test after the administration of vitamin K.
† Given intravenously.

COMMON DUCT OBSTRUCTION DUE TO CALCULUS

The 13 patients with obstruction of the common duct due to calculus had prothrombin levels varying between 30 and 100 per cent of normal. The average level for the group was 75 per cent. In none of the cases was bleeding evident. The response to vitamin K was rapid (table 2), even though the biliary cirrhosis observed at operation was frequently severe.

STRICTURE OF THE COMMON DUCT

The 2 patients with stricture of the common duct had prothrombin levels of 16 and 26 per cent (table 3). Both patients had complete obstruction of the common duct of long standing and apparently had received some bile salts prior to admission, although they denied having

had medication of any kind during three weeks before they entered the hospital. In these cases the condition was more severe than in the two preceding groups. As was to be expected, the prothrombin levels were lower and the biliary cirrhosis more marked. Patients who have some bile entering the duodenum (stenosis without complete obstruction) naturally show higher prothrombin levels.

TABLE 2.—*Cases of Obstruction of the Common Duct Due to Calculus*

	Prothrombin Level, Percentage of Normal				Treatment		
Case	Initial	After Vitamin K	Final	Highest Icteric Index	Hours Between Tests *	Vitamin K, Mg.	Bile Salts, Gm.	Comment
1	30	97	100	17	48	8	2.56	
2	44	92	100	60	24	8	1.28	
3	50	95	100	101	48	6	1.28	
4	50	90	72	65	48	4	0.96	Level decreased because of biliary drainage
5	75	100	88	45	18	8	0.64	
6	77	95	100	90	48	5†	0	Biliary cirrhosis marked
7	80	...	...	60	..	..	....	Patient refused operation
8	86	96	100	24	24	4	0.64	
9	87	100	100	29	24	4	0.96	
10	93	...	100	30	..	0	0	
11	100	...	100	45	..	0	0	Icteric for only 2 days
12	100	...	100	36	..	0	0	Partial and intermittent biliary obstruction
13	100	...	100	25	..	0	0	Intermittent mild icterus for 3 mo.

* Hours between initial prothrombin test and test after the administration of vitamin K.
† Given intravenously.

TABLE 3.—*Cases of Obstruction of the Common Duct Due to Stricture*

	Prothrombin Level, Percentage of Normal				Treatment		
Case	Initial	After Vitamin K	Final	Highest Icteric Index	Hours Between Tests *	Vitamin K, Mg.	Bile Salts, Gm.	Comment
1	16	100	...	190	20	8	1.28	Severe biliary cirrhosis
2	20	88	90	65	24	10	1.92	Severe biliary cirrhosis

* Hours between initial prothrombin test and test after the administration of vitamin K.

BILIARY FISTULA

The 5 patients with biliary fistula (table 4) showed prothrombin levels between 35 and 93 per cent of normal with an average of 61 per cent. In this type of case, the prothrombin level usually varies directly with the duration of the fistula, provided hepatic damage has not been severe and the bile loss has been complete. The response to therapy with vitamin K and bile salts is usually uniformly good.

BURNS

The series of cases of burns is too small to be conclusive, but it seems that the prothrombin test should be useful in formulating a prognosis.

In table 5, patient 1 was admitted to the hospital and given the usual therapy for burns (débridement and tannic acid spray). The first blood sample, which was taken twelve hours after the patient had been burned, showed slight icterus; this gradually rose to 58 on the third day in the hospital, or the day prior to death. Twenty-four hours after admission, the patient began vomiting small amounts of blood. He gradually became confused and disoriented. His urinary output continued to be

TABLE 4.—*Cases of Biliary Fistula*

Case	Prothrombin Level, Percentage of Normal: Initial	After Vitamin K	Final	Highest Icteric Index	Hours Between Tests *	Treatment: Vitamin K, Mg.	Bile Salts, Gm.	Comment
1	35	96	100	7	20	8	1.28	Biliary fistula for 3 to 4 mo. before patient entered hospital
2	45	...	100	17	..	..	....	Level rose gradually with 1.28 Gm. bile salts three times per day
3	64	98	100	29	48	4	0.96	Moderate biliary cirrhosis present
4	70	100	100	...	48	12	1.92	Patient had some bile salts before entering hospital
5	93	100	100	5	..	..	0.64	Bile apparently entered gastrointestinal tract until about 1 week before admission

* Hours between initial prothrombin test and test after the administration of vitamin K.

TABLE 5.—*Cases of Severe Burns*

Case	Prothrombin Level, Percentage of Normal: Initial	After Vitamin K	Final	Highest Icteric Index	Hours Between Tests *	Treatment: Vitamin K, Mg.	Bile Salts, Gm.	Comment
1	8	8	8	58	24	5	0	Autopsy revealed severe liver necrosis and blood in the gastrointestinal tract
2	17	...	...	112	..	0	0	Autopsy showed severe liver necrosis
3	94	...	100	16	..	0	0	Icteric index fell to 6 with improvement

* Hours between initial prothrombin test and test after the administration of vitamin K.

good, and the blood urea nitrogen determinations gave normal values. He was treated adequately with fluids and plasma but became more comatose, and hematemesis increased. On the third day in the hospital, the prothrombin level was 8 per cent of normal. Five milligrams of vitamin K was given intravenously without any effect on the prothrombin blood level. He died twenty hours later, and autopsy showed extreme necrosis of the liver and blood throughout the lumen of the gastrointestinal tract. No one bleeding point could be identified, and no areas of ulceration were seen. In the second case, the prothrombin level fell to 17 per cent before the death of the patient, and at autopsy marked

TABLE 6.—*Cases of Intestinal Disorders*

Case	Prothrombin Level Percentage of Normal: Initial	After Vitamin K	Final	Hours Between Tests *	Treatment: Vitamin K, Mg.	Bile Salts, Gm.	Diagnosis	Comment
1	6	100	100	14	6	0.96	Intestinal obstruction	After 2 weeks of intestinal intubation profuse gastrointestinal bleeding started; it stopped with vitamin K
2	18	82	100	24	8	0	Intestinal obstruction and postoperative intestinal fistula	Oozing of blood from wound on eighth postoperative day
3	20	...	...	..	0	0	Perforated gastric ulcer; subphrenic abscess	On gastrointestinal suction and no food there was bleeding from wound; patient died before vitamin K could be given
4	20	88	100	12	8	1.28	Strangulated ventral hernia	On intestinal intubation for 15 days there were bloody stools; bleeding was stopped with vitamin K
5	21	7b	100	22	4	0	High intestinal fistula	Bleeding from the wound stopped with treatment
6	22	82	100	24	8	0	Pneumonia; peritonitis; intestinal obstruction	Gastrointestinal bleeding and bleeding from wound responded to vitamin K therapy
7	26	51	100	12	8	0	Intestinal obstruction	Prothrombin level of 100 per cent occurred 40 hours after vitamin K was given; intestinal intubation used
8	34	82	87	24	4	0.32	Appendicitis; term pregnancy, delivered; fecal fistula	Intestinal intubation used
9	38	80	100	20	8	1.28	Low postoperative intestinal fistula	Intestinal intubation used
10	38	80	100	18	8	1.28	Adenocarcinoma of the stomach	Bleeding from wound was moderate on sixth postoperative day; gastric suction employed
11	50	80	93	48	10	0	Appendicitis with perforation and peritonitis	Poor diet and gastric suction; bleeding from wound; blood transfusion prior to prothrombin test; no bleeding after administration of vitamin K
12	60	...	95	..	0	0	Adenocarcinoma of the stomach	Gastric suction and no food; level returned to normal when food was given and suction stopped
13	62	...	100	..	0	0	Carcinoma of the sigmoid; intestinal fistula	Had been on starvation diet
14	66	...	85	..	0	0	Intestinal obstruction	Intestinal intubation for 6 days prior to test; level returned toward normal as food was given
15	70	...	95	..	0	0	Perforated gastric ulcer	Twenty-one days of inadequate diet and intermittent gastric suction
16	70	...	...	..	0	0	Diverticulitis of the colon	Severe diarrhea

16	70	...	...	..	0	0	Diverticulitis of the colon.....	Severe diarrhea
17	70	100	100	24	4	0	Intestinal obstruction	Intestinal intubation had been employed
18	72	...	100	..	0	0	Pyloric obstruction due to chronic granulomatous gastritis	Level determined 6 days after gastric resection returned to normal with food
19	74	...	100	..	0	0	Chronic gastric ulcer with pyloric obstruction	Preoperative level was 98 per cent; level fell with gastric suction and inadequate diet
20	75	...	100	..	0	0	Acute appendicitis with perforation and peritonitis	Two days after operation the prothrombin level was 92 per cent; it fell owing to lack of food and gastric suction
21	76	...	...	..	0	0	Carcinoma of the rectum and malnutrition	Inadequate diet; test made 13 days after operation
22	77	...	100	..	0	0	Carcinoma of the colon; low intestinal fistula	On poor diet
23	80	94	100	24	2	0.32	Chronic gastric ulcer with pyloric obstruction	Patient had marked vomiting prior to admission
24	86	...	...	..	0	0	Nontropical sprue	Marked diarrhea present
25	88	...	100	..	0	0	Acute appendicitis; bleeding peptic ulcer	One day after appendectomy, the patient vomited 1,000 cc. of blood
26	90	...	...	..	0	0	Severe ulcerative colitis.....	Marked malnutrition and diarrhea
27	90	...	100	..	0	0	Carcinoma of the stomach with pyloric obstruction	After gastroenterostomy with inadequate diet and suction, level fell to 72 per cent
28	93	...	100	..	0	0	Intestinal obstruction; appendical abscess	Intubation and poor diet
29	93	100	100	24	4	0	Gastrocolic fistula	Patient showed marked weight loss
30	95	...	...	..	0	0	Partial intestinal obstruction; malnutrition	
31	100	...	...	..	0	0	Carcinoma of the stomach.....	Poorly nourished
32	100	...	...	..	0	0	Intestinal obstruction	Gastric suction was employed for 3 days; then diet was started; prothrombin level determined on fifth postoperative day
33	100	...	...	..	0	0	Nontropical sprue	
34	100	...	100	..	0	0	Severe ulcerative colitis.....	Prothrombin levels taken 2 months apart during severe illness
35	100	...	...	..	0	0	Gastrojejunocolic fistula	Patient had lost 51 pounds
36	100	...	...	..	0	0	Duodenal ulcer with hemorrhage.....	

* Hours between initial prothrombin test and test after the administration of vitamin K.

liver necrosis was again present. The third patient was a man who had been burned almost as extensively as either of the first 2 patients. His prothrombin level fell slightly when his icteric index was showing a slight rise; as he improved, both returned to normal.

INTESTINAL DYSFUNCTION

Thirty-six patients with intestinal dysfunction were studied. The prothrombin levels varied between 6 and 100 per cent of normal (table 6). A wide variety of cases is presented in this series, but for the most part the patients who showed the most profound changes were those with small intestinal fistulas or intestinal intubation. (Cases 1, 3, 4, 5, 6, 7 and 22 were previously reported at greater length, and a more complete discussion of this type of disorder was presented.[1c]) Usually, these patients show an adequately functioning liver, and the deficiency of prothrombin is due to an inadequate diet, loss of bile or a malfunctioning gastrointestinal tract.

MISCELLANEOUS CASES

Five patients with heart disease with decompensation showed levels between 55 and 94 per cent. In 2 of these, postmortem examination showed marked chronic passive congestion of the liver. Ten patients with severe gallbladder disease had prothrombin levels between 90 and 100 per cent, and it is thought that patients with uncomplicated cholecystitis and cholelithiasis rarely show values below this.

Four patients with hepatitis and 4 with catarrhal jaundice were observed; these showed levels ranging between 52 and 100 per cent of normal. Some of these patients responded to vitamin K and bile salts, and it was believed that the deficiency was due largely to the fact that although liver function was adequate, bile could not enter the duodenum because of the swelling causing intrahepatic biliary obstruction.

A patient with Weil's disease was tested. He had previously had fairly severe nasal hemorrhages, but unfortunately the first prothrombin level was obtained about one week later and was then 85 per cent of normal. Another patient with numerous congenital cysts of the liver had a prothrombin level of 81 per cent, and a patient with a bullet wound of the liver showed a prothrombin level of 92 per cent. Neither of these patients responded to vitamin K therapy.

Four patients were seen because of bleeding, and prothrombin levels were determined. For 2 of these patients, the diagnosis was thrombopenic purpura; for the other 2, hemophilia. Prothrombin levels of 100 per cent were found in each instance. A man receiving large amounts of heparin because of recent pulmonary embolus had a prothrombin level of 100 per cent, even though his clotting time was greatly prolonged.

Recently, Sheely [5] reported lowering of the prothrombin level in slightly less than 50 per cent of the tuberculous patients he studied. In the 4 cases in our series, 2 patients had severe recurrent pulmonary hemorrhages due to extensive tuberculosis of the lungs, and 2 had widespread miliary tuberculosis. Both of the patients with hemorrhage had prothrombin levels above the bleeding zone (85 and 97 per cent), but vitamin K was nevertheless administered. Hemoptysis was not altered in either case. In the 2 other patients with levels of 52 and 86 per cent, autopsy showed moderate liver disease along with diffuse miliary tuberculosis.

COMMENT

In the cases presented, the patients with leukemia, cirrhosis and burns failed to show any response to vitamin K therapy owing to hepatocellular damage. In several instances, the prothrombin levels of patients with extensive tumor metastases to the liver with accompanying biliary cirrhosis did not show any improvement with adequate therapy with vitamin K and bile salts. Lord and Andrus [6] recently advocated the determination of the prothrombin blood level as an aid in differentiating intrahepatic and extrahepatic jaundice. Prior to this, Scanlon and associates,[7] Stewart [8] and other workers produced evidence to show that such diseases as cirrhosis, hepatitis and leukemia are accompanied by low prothrombin levels solely because of liver damage. Wilson [9] showed that in such cases the results of the hippuric acid test of liver function are closely correlated with the prothrombin blood level. Most of the numerous liver tests available today merely indicate the degree of liver function present; on the other hand, serial determinations of the prothrombin amount not only give one an idea of the degree of damage that may be present but also aid greatly in the differential diagnosis of intrahepatic and extrahepatic jaundice.

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5. Sheely, R. F.: Prothrombin Deficiency in Pulmonary Tuberculosis, J. A. M. A. **117**:1603-1606 (Nov. 8) 1941.

6. Lord, J. W., Jr., and Andrus, W. deW.: Differentiation of Intrahepatic and Extrahepatic Jaundice, Arch. Int. Med. **68**:199-210 (Aug.) 1941.

7. Scanlon, G. H.; Brinkhous, K. M.; Warner, E. D.; Smith, H. P., and Flynn, J. E.: Plasma Prothrombin and Bleeding Tendency with Special Reference to Jaundiced Patients and Vitamin K Therapy, J. A. M. A. **112**:1898-1901 (May 13) 1939.

8. Stewart, J. D.: Prothrombin Deficiency and Effects of Vitamin K in Obstructive Jaundice and Biliary Fistula, Ann. Surg. **109**:588-595 (April) 1939.

9. Wilson, S. J.: Quantitative Prothrombin and Hippuric Acid Determinations as Sensitive Reflectors of Liver Damage in Human Subjects, Proc. Soc. Exper. Biol. & Med. **41**:559-561 (June) 1939.

Unless the liver function can be improved in cases with hepatocellular damage, the low prothrombin level will remain unchanged or decrease further, even though large quantities of vitamin K and bile salts are given.

Wolff, Elkinton and Rhoads [10] in studying cases of burns by various liver function tests showed a lowering of the prothrombin level corresponding to the decrease in the liver function. In their series, all the patients recovered, and none showed prothrombin levels in the bleeding zone. In cases of burns, therefore, it is thought that the prothrombin test is a rather accurate index of liver damage, and in the event that the prothrombin level decreases rapidly, the prognosis is grave. Such patients with liver necrosis will not respond to the administration of vitamin K.

Some patients with acute hepatitis and catarrhal jaundice show low prothrombin levels because of liver damage and apparently also because of obstruction due to congestion and swelling in the small intrahepatic bile channels. The extent and rate of response to vitamin K in such patients points out which factor is the most important. Although we have not seen a patient with hepatitis or catarrhal jaundice that progressed to acute yellow atrophy, it seems that the prothrombin level in such a patient should continue to fall and not respond to vitamin K therapy. In Weil's disease, the prothrombin level probably reacts similarly to the way it does in cases of hepatitis or catarrhal jaundice.

Practically all patients with biliary obstruction due to stone, tumor or scar tissue responded to adequate amounts of vitamin K in twenty-four to forty-eight hours. One patient did not, and 2 others who showed a normal response initially later failed to show a rise with adequate amounts of treatment. In all 3, autopsy revealed obstruction of the common duct with severe biliary cirrhosis and extensive liver metastasis. It is believed that the condition would have to be severe before only one of the two aforementioned disorders would result in persistent hypoprothrombinemia when vitamin K had been administered. In cases of mild or moderate involvement, the response to vitamin K might be slower than normal, but it should occur.

In patients with tuberculosis, it is probable that hemoptysis does not occur owing to hypoprothrombinemia, but it might be exaggerated when the blood-clotting mechanism is subnormal. In the cases presented, tuberculosis was severe, but, of course, the number is too small to permit any definite conclusions.

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10. Wolff, W. A.; Elkinton, J. R., and Rhoads, J. E.: Liver Damage and Dextrose Tolerance in Severe Burns, Ann. Surg. **112**:158-160 (July) 1940.

CONCLUSIONS

A brief summary is presented of 120 cases which were studied during the past two and one-half years. The importance of keeping hypoprothrombinemia in mind in cases in which various types of intestinal disorders are present is stressed.

The prothrombin test, which can be simply done and is inexpensive, is an aid in determining the type of jaundice. It is necessary to study the patients carefully and repeatedly both before and after the administration of vitamin K and to be well acquainted with their complaints and physical findings in order that the results can be properly evaluated. In the series presented, it has been shown that patients with relatively severe liver damage do not respond to vitamin K therapy and that patients with common duct obstruction practically always respond to adequate therapy.

Finally, it apparently is a test which can help the physician determine the severity of liver damage in cases of burns, and it is thought that by serial examinations, an early and accurate prognosis can be formulated.

EFFECT OF DESOXYCORTICOSTERONE ACETATE IN POSTOPERATIVE SHOCK

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In recent years there have been several attempts made to apply some of the experimental methods for the prevention of shock in animals to practical use in human beings. Many of these have taken the form of direct replacement of liquid to make up for the loss of circulating blood volume. Others have depended on the use of adrenocortical substances, for the value of which some observers [1] have made important claims.

That adrenocortical substances might have considerable value in the prevention or the treatment of shock is suggested by a large amount of clinical, pathologic and experimental data gathered by many different observers. Thus Short [2] suggested the theory that failure of the adrenal glands, which play an important role in the maintenance of vessel tone, precipitates the state of shock. Swingle and associates [3] showed that adrenalectomized dogs maintained in normal health and vigor by injections of adrenal cortical extract lapsed into circulatory collapse and shock following any trauma which put a strain on them. They suggested the similarity of the signs and symptoms of adrenal insufficiency and traumatic shock. Selye and associates [4] found characteristic changes in

1. (*a*) Wilson, W. C.; MacGregor, A. R., and Stewart, C. P.: The Clinical Course and Pathology of Burns and Scalds Under Modern Methods of Treatment, Brit. J. Surg. **25**:826, 1938. (*b*) Perla, D.; Freiman, D. G.; Sandberg, M., and Greenberg, S. S.: Prevention of Histamine and Surgical Shock by Cortical Hormone (Desoxycorticosterone Acetate and Cortia) and Saline, Proc. Soc. Exper. Biol. & Med. **43**:397, 1940. (*c*) Reed, F. R.: Acute Adrenal Cortex Exhaustion and Its Relationship to Shock, Am. J. Surg. **40**:514, 1938. (*d*) Besser, E. L.: Role of the Adrenal Glands in Shock, Arch. Surg. **43**:249 (Aug.) 1941.

2. Short, R., in Mekie, E. C.: Handbook of Surgery, Baltimore, William Wood & Company, 1936, p. 35.

3. Swingle, W. W., and others: Effect of Priming Doses of Desoxycorticosterone Acetate in Preventing Circulatory Failure and Shock in Adrenalectomized Dog, Am. J. Physiol. **132**:249, 1941. Swingle, W. W.; Parkins, W. M.; Taylor, A. R., and Hays, H. W.: A Study of the Circulatory Failure and Shock Following Trauma to the Healthy Vigorous Adrenalectomized Dog, ibid. **124**:22, 1938.

4. Selye, H.; Dosne, C.; Bassett, L., and Whittaker, J.: Value of Cortical Hormones in Traumatic Shock and Allied Conditions, Canad. M. A. J. **43**:1 (July) 1940. Selye, H., and Dosne, C.: Changes (Hypochloremia and Adrenal Atrophy) Produced by Desoxycorticosterone Overdosage in Rat, Proc. Soc. Exper. Biol. & Med. **44**:165, 1940.

the adrenal glands during shock and showed the increased activity of the adrenal glands during recovery. The findings of Zwemer [5] and the results of Wohl and co-workers [6] also showed pathologic changes in the adrenal cortex in conditions associated with shock. Weil and Browne [7] found large quantities of adrenal cortical hormone in the urine of patients after operation; they interpreted this as suggesting an effort of these glands to overcome operative shock.

According to Thorn and associates,[8] Cleghorn and associates,[9] Levy Simpson [10] and Loeb and associates,[11] adrenal cortical hormone affects electrolyte and water metabolism. It causes striking retention of sodium salts with restoration of the blood sodium level to normal. It causes also retention of water with increase in plasma and interstitial fluid volume and consequent gain in weight. It lowers the serum potassium, at times to abnormally low levels, and temporarily increases the excretion of this ion. It restores renal function and increases the excretion of nitrogen when nonprotein nitrogen has been retained. It causes also a decrease in the concentration of total protein, calcium and cholesterol in the serum, probably because of hemodilution associated with an increase in plasma volume.

By the use of adrenal cortical extract, Heuer and Andrus [12] prolonged the lives of dogs in which shock was produced by the intravenous injection of aqueous extracts of obstructed intestinal loops. Menkin [13] reported that the increase in capillary permeability caused by inflam-

5. Zwemer, R. L.: Study of Adrenal Cortex Morphology, Am. J. Path. **12**: 107, 1936.

6. Wohl, M. G.; Burns, J. C., and Clark, J. H.: Adrenal Glands in Dogs with High Intestinal Obstruction, Proc. Soc. Exper. Biol. & Med. **33**:543, 1936.

7. Weil, P., and Browne, J. S. L.: The Excretion of Cortin After Surgical Operations, Science **90**:445, 1939.

8. Thorn, G. W.; Howard, R. P., and Emerson, K., Jr.: Treatment of Addison's Disease with Desoxycorticosterone Acetate, a Synthetic Adrenal Cortical Hormone, J. Clin. Investigation **18**:449, 1939.

9. Cleghorn, R. A.; Fowler, J. L. A., and Wenzel, J. S.: The Assay of Desoxycorticosterone Acetate and Its Use in the Treatment of Addison's Disease, J. Clin. Investigation **18**:475, 1939.

10. Levy Simpson, S.: The Use of Synthetic Desoxycorticosterone Acetate in Addison's Disease, Lancet **2**:557, 1938.

11. Loeb, R. F.; Atchley, D. W.; Ferrebee, J. W., and Ragan, C.: Observations on the Effect of Desoxycorticosterone Esters and Progesterone in Patients with Addison's Disease, Tr. A. Am. Physicians **54**:285, 1939.

12. Heuer, G. J., and Andrus, W. DeW.: Effect of Adrenal Cortical Extract in Controlling Shock Following Injection of Aqueous Extracts of Closed Intestinal Loops, Ann. Surg. **100**:734, 1934.

13. Menkin, V.: Effect of Adrenal Cortex Extract on Capillary Permeability, Am. J. Physiol. **129**:691, 1940.

matory exudates can be wholly or in part inhibited by the local injection of adrenal cortical extract and separately by desoxycorticosterone acetate.

McAllister and Thorn [14] found that the decrease in plasma volume during shock could be prevented in dogs by large intravenous doses of adrenal cortical extract. Fine and associates [15] showed that although a decrease in plasma volume was lessened in dogs subjected to a distention of the small intestine by the use of desoxycorticosterone acetate, the survival time was not appreciably increased. Wilson and co-workers [18] reported favorable results from the use of adrenal cortical extracts in shock following burns.

McAllister [16] and, separately, Ragan and co-workers [17] showed that desoxycorticosterone esters administered three to six hours before operation prevent the usual decrease in plasma volume accompanying the administration of ether and surgical operations in dogs. Perla and associates [1b] expressed the belief that histamine shock in rats and mice could be prevented by treatment with adrenal cortical extract and solution of sodium chloride.

Such data naturally led to the application of the method to the treatment of shock in human beings.[18] The appearance of reports of the results (which will be discussed later) led us to try the method in selected operative patients.

There are obvious difficulties in establishing satisfactory criteria for the evaluation of the therapy. Many factors, such as the previous condition of the patient, the location and the extent of the lesion, the anesthesia, the duration of the operation, the amount of blood loss, the vomiting, the temperature, the degree of fluid loss by evaporation or diarrhea or emesis, contribute to the postoperative picture. The significance of blood pressure drop or the degree of hemoconcentration demands fractional evaluation of the amount of blood loss and of other fluid loss during and after the operation; both evaluations introduce large errors. In a recent discussion of the applicability of experimental results

14. McAllister, F. F., and Thorn, G. W.: Effect of Adrenal Cortical Hormone on Reduction of Plasma Volume Resulting from Etherization, Proc. Soc. Exper. Biol. & Med. **36**:736, 1937.

15. Fine, J.; Fuchs, F., and Mark, J.: Effect of Desoxycorticosterone on Plasma Volume in Intestinal Obstruction, Proc. Soc. Exper. Biol. & Med. **43**:514, 1940.

16. McAllister, F. F.: The Effect of Ether Anesthesia on the Volume of Plasma and Extracellular Fluid, Am. J. Physiol. **124**:391, 1938.

17. Ragan, C.; Ferrebee, J. W., and Fish, G. W.: Effect of Desoxycorticosterone Acetate on Plasma Volume in Patients During Ether Anesthesia and Surgical Operation, Proc. Soc. Exper. Biol. & Med. **42**:712, 1939.

18. (*a*) Brown, J. J. M.; Dennison, W. M.; Ross, J. A., and Divine, D.: Experiences at a Casualty Clearing Station, Lancet **2**:443, 1940. (*b*) Footnote 1.

to the problem of shock in man, Wiggers [19] called attention to the desirability of establishing reliable criteria which indicate that a state has been produced which is similar to that observed in traumatic, surgical and toxemic shock of man. He pointed out also that the term "shock" should perhaps be restricted to an irreversible state of circulatory failure.

Since the ultimate aim in the prevention of shock or its early recognition and treatment is the avoidance of death, we decided to use the mortality rate as the criterion of the efficacy of the therapy. This would give greater objectivity and enable us to avoid relying on clinical impressions alone. This is especially true if the use of the term "shock" is restricted to irreversible circulatory collapse, since it must then be reflected in the total mortality rate.

TABLE 1.—*Distribution of Operative Procedures Performed on Control and Treated Patients*

Operation	Treated with Desoxycorticosterone Acetate		Controls	
	Number	Deaths	Number	Deaths
Radical mastectomy	15	0	15	0
Gastrectomy	38	4	38	3
Abdominoperineal resection of rectum	11	2	11	1
Resection of colon	10	2	10	1
Ileosigmoidostomy	1	0	1	0
Colostomy	3	0	3	0
Obstructive resections	1	0	1	0
Resection for regional enteritis	5	1	5	1
Splenectomy	1	0	1	0
Thoracoplasty for tuberculosis	1	0	1	0
Nephrectomy for carcinoma	1	0	1	0
Perforated gastroduodenal ulcer	2	0	2	0
Cholecystenterostomy	2	0	2	1
Excision of retroperitoneal sarcoma	1	0	1	0
Thoracotomy for excision of sarcoma of the thorax	1	1	1	1
Cholecystectomy and choledochostomy with T tube; previous acute pancreatitis	1	0	1	0
Amputation of leg	1	0	1	0
Laparotomy for carcinoma of stomach	1	0	1	1
Anterior gastrojejunostomy for carcinoma	1	0	1	0
Cholecystectomy and choledochostomy with T tube for acute pancreatitis and cholelithiasis	3	1	3	0
Total	100	11	100	9

EXPERIMENTAL

To establish reliable controls, alternate patients were chosen to the number of 200. Since the value of the therapy could not be determined if given to patients who manifestly would not need it (e. g., those with hernias, hysterectomies or vaginal plastics), only patients with lesions of graver nature were chosen. In the control and the treated group there were equal numbers of patients for the various operative procedures (table 1). All operations were performed with the patient under spinal anesthesia.

19. Wiggers, C. J.: Physiology in Health and Disease, Philadelphia, Lea & Febiger, 1939, p. 742.

TABLE 2.—*Data on Treated and Control Patients Subjected to Radical Mastectomy*

Treated Group					Control Group				
Fifteen patients with carcinoma of the breast were given desoxycorticosterone acetate and intravenous injections of 5 per cent dextrose in physiologic solution of sodium chloride before and after operation. There were no deaths. All the patients were women.					Fifteen control patients were given ordinary preoperative and postoperative intravenous injections of 5 per cent dextrose in physiologic solution of sodium chloride. There were no deaths. All the patients were women.				
	Administration of Desoxycorticosterone Acetate					Intravenous Administration of Dextrose-Saline Solution			
Age *	Days Preoperative	Days Postoperative	Days in Hospital †	Complications	Age *	Days Preoperative	Days Postoperative	Days in Hospital †	Complications
36	1	12	17	None	49	1	2	15	None
55‡	1	12	21	None	60‡	1	2	16	None
30	1	12	19	None	26	1	2	25	None
49	1	12	23	None	34	1	2	19	None
41	1	12	16	None	45	1	2	14	None
41	1	12	17	None	44	1	2	20	None
66	1	12	19	None	67	1	2	21	None
59‡	1	12	22	None	55‡	1	2	17	None
37	2	12	15	None	45	1	2	18	None
40	1	12	15	None	48	1	2	16	None
35	2	12	17	None	45	1	2	17	None
56	1	12	19	None	49	1	2	17	None
52	2	11	17	None	54	1	2	17	None
49	2	10	17	Pneumonia in the left lower lobe	46	1	2	18	None
39	1	12	18	None	45	1	2	18	None

* Average age: treated group, 45.6; control group, 46.3 years.

† Average days in hospital: treated group, 17.9; control group, 17.5.

‡ Condition only fair.

TABLE 3.—*Data on Treated and Control Patients Subjected to Gastrectomy for Carcinoma*

Treated Group

Eighteen patients were given desoxycorticosterone acetate intramuscularly and 5 per cent dextrose in physiologic solution of sodium chloride intravenously before and after operation. Thirteen patients were only fair risks; 5 were good risks; 2 deaths occurred.

Age *	Sex	Administration of Desoxycorticosterone Acetate: Days Pre-operative	Administration of Desoxycorticosterone Acetate: Days Post-operative	Days in Hospital †	Complications
59	F	2	12	18	None
71	M‡	1	14	19	Pneumonia in the right lower lobe
46	M§	2	14	20	None
67	M‡	2	14	17¶	Cerebral hemorrhage
48	M	2	14	19	None
62	M‡	1	13	18	Bilateral broncho-pneumonia
58	M‡	1	14	17	None
60	F‡	2	11	16	None
60	M‡	2	12	16	None
42	M‡	1	13	23	None
43	M	2	14	21	None
66	F‡	2	7	11¶	Bilateral bronchopneumonia with cardiac decompensation
66	M‡	2	13	23	None
64	M‡	2	13	15	None
55	M‡	1	14	21	None
53	F‡‖	3	11	14	None
44	M	1	13	16	None
62	M‡	1	13	15	None

Control Group

Eighteen control patients were given 5 per cent dextrose in physiologic solution of sodium chloride intravenously before and after operation. Thirteen patients were only fair risks; 5 were good risks; 1 death occurred.

Age *	Sex	Intravenous Administration of Dextrose-Saline Solution: Days Pre-operative	Intravenous Administration of Dextrose-Saline Solution: Days Post-operative	Days in Hospital †	Complications
63	F	1	3	18	None
77	F‡	1	3	18	None
51	M	2	3	18	Pneumonia in the left lower lobe
50	M‡	2	3	17	None
69	M	1	3	16	None
71	M‡	2	3	15	None
65	F‡	1	3	18	None
59	M§	2	2	18	None
59	M‡	2	3	17	None
65	F‡	1	2	20	None
43	M§	1	3	17	None
57	M§	1	4	5¶	Peritonitis
71	F‡	1	2	19	None
64	M‡§	2	3	15	None
51	F‡	1	2	14	None
58	M‡§	1	2	14	None
44	M§	2	2	17	None
55	F‡	1	2	15	None

* Average age: treated group, 57.5; control group, 58.9 years.
† Average days in hospital (not including patients who died): treated group, 18.1; control group, 16.8.
‡ Fair risk.
§ Ulcer found on pathologic study.
‖ Sarcoma found on pathologic study.
¶ Patient died.

TABLE 4.—*Data on Patients Subjected to Gastrectomy for Ulcer*

Treated Group						Control Group					
Twenty patients were given desoxycorticosterone acetate and 5 per cent dextrose in physiologic solution of sodium chloride before and after operation. There were 2 deaths.						Twenty control patients were given 5 per cent dextrose in physiologic solution of sodium chloride before and after operation. There were 2 deaths.					
		Administration of Desoxycorticosterone Acetate						Intravenous Administration of Dextrose-Saline Solution			
Age *	Sex	Days Pre-operative	Days Post-operative	Days in Hospital †	Complications	Age *	Sex	Days Pre-operative	Days Post-operative	Days in Hospital †	Complications
56	F	1	13	15	None	41	M	2	2	15	None
47	M	2	13	16	None	52	M	3	3	17	None
44	M	2	3	18	Pneumonia in the left lower lobe	25	M	2	5	16	None
46	M	1	16	18¶	Pulmonary embolism	63	M	1	3	4¶	Bronchopneumonia and cardiac decompensation
42	M	2	12	17	None	53	M§	1	3	14	None
31	F‡	1	12	17	None	38	M‡	1	4	16	None
46	M‡	1	16	38	Pneumonia in the left lower lobe	68	F‡	1	2	17	None
47	M‡	2	13	14	None	55	M‡	1	2	14	None
55	M	2	17	21	None	62	M§	1	3	15	None
50	M	3	3	6¶	Cerebral thrombosis with hemiplegia and cardiac decompensation	44	M	1	5	16¶	Pulmonary embolism
46	M	2	13	15	None	41	M	1	3	16	None
39	F	2	10	21	None	38	M	1	2	12	None
45	M	2	13	15	None	43	M§	1	3	16	None
37	M	3	13	21	None	54	M	2	2	18	None
36	M	2	10	15	None	43	M	1	3	16	None
33	F	2	10	16	None	44	M	1	3	16	None
30	M	2	11	16	None	33	M	2	3	16	None
55	M	2	10	20	None	46	M§	1	3	17	None
59	F	3	11	22	None	40	M	2	3	18	None
57	M‡	2	10	16	None	49	M‡	2	2	17	None

* Average age: treated group, 45.1; control group, 46 6 years.
† Average days in hospital (not including those who died): treated group, 18.5; control group, 15.8.
‡ Fair risk (4 patients in each group).
§ Carcinoma found on pathologic study (4 cases in control group).
¶ Patient died.

§ Carcinoma found on pathologic study (4 cases in control group).
¶ Patient died.

TABLE 5.—*Data on Treated and Control Patients Subjected to Abdominoperineal Resection of the Rectum for Carcinoma*

Treated Group: Eleven patients were given desoxycorticosterone acetate intramuscularly and 5 per cent dextrose in physiologic solution of sodium chloride intravenously before and after operation. There were 2 deaths.						Control Group: Eleven control patients were given 5 per cent dextrose in physiologic solution of sodium chloride intravenously before and after operation. There was 1 death.					
		Administration of Desoxycorticosterone Acetate						Intravenous Administration of Dextrose-Saline Solution			
Age *	Sex	Days Pre-operative	Days Post-operative	Days in Hospital †	Complications	Age *	Sex	Days Pre-operative	Days Post-operative	Days in Hospital †	Complications
62	M	2	13	38	None	40	M	1	2	37	None
65	M‡	1	14	30	None	63	F‡	1	2	18	None
55	F	1	12	26	None	52	M	1	2	18	None
28	F	1	14	34	None	42	F	2	2	31	None
64	F‡	3	13	60	Bilateral bronchopneumonia	81	F‡	2	3	30	None
60	M‡	2	14	36	None	66	F‡	2	3	34	None
45	F	1	12	35	None	71	M	2	2	37	None
56	F‡	3	7	10¶	Cerebral hemorrhage and cardiac decompensation	61	M‡	1	3	24	Pneumonia in the left lower lobe
60	M‡	2	13	48	Pneumonia in the right lower lobe	55	F‡	2	2	42	None
63	F‡	2	13	49¶	Pulmonary embolism	68	M‡	2	3	9¶	Bilateral bronchopneumonia and cardiac decompensation
73	M‡	2	10	39	None	66	F‡	2	2	41	None

* Average age: treated group, 59.1; control group, 60.4 years.
† Average days in hospital (not including patients who died): treated patients, 34.8; control patients, 31.2.
‡ Condition only fair.
¶ Patient died.

TABLE 6.—*Data on Treated and Control Patients Subjected to Resection of the Colon for Carcinoma*

Treated Group						Control Group					
Ten patients were given desoxycorticosterone acetate intramuscularly and 5 per cent dextrose in physiologic solution of sodium chloride intravenously before and after operation. There were 2 deaths.						Ten control patients were given 5 per cent dextrose in physiologic solution of sodium chloride. There was 1 death.					
		Administration of Desoxycorticosterone Acetate						Intravenous Administration of Dextrose-Saline Solution			
Age *	Sex	Days Pre-operative	Days Post-operative	Days in Hospital †	Complications	Age *	Sex	Days Pre-operative	Days Post-operative	Days in Hospital †	Complications
58	M‡§	2	17	34	None	68	F‡‖	1	3	31	None
55	M‡‖	2	7	9¶	Peritonitis	55	F‡‖	1	2	43	None
66	F‡‖	2	14	50	None	52	F‡‖	2	3	39	None
64	M‡	1	3	4¶	Coronary occlusion and bilateral bronchopneumonia	53	F‡	1	3	20	None
59	F‡	1	14	43	Pneumonia in the right lower lobe	43	M‡	1	3	26	None
58	M‡	3	14	24	None	65	F‡	1	2	10	None
67	F‡‖	2	14	30	Fecal fistula	70	M‡‖	4	3	21¶	Bilateral bronchopneumonia
52	M	1	18	28	None	45	F	2	3	18	None
47	M‡§	1	23	51	None	50	F‡§	1	2	42	None
57	M‡	2	14	19	None	43	M‡	1	3	25	None

* Average age: treated group, 57.3; control group, 55.3 years.
† Average days in hospital (not including patients who died): treated group, 34.8; control group, 29.2.
‡ Fair risk.
§ Primary cecostomy with subsequent resection.
‖ Exteriorization.
¶ Patient died.

Treated Group	Control Group
Desoxycorticosterone acetate was given twice daily intramuscularly with intravenous injections twice daily of 5 per cent dextrose in physiologic solution of sodium chloride before and after operation.	Twice daily 5 per cent dextrose in physiologic solution of sodium chloride was given intravenously before and after operation.

Treated Group: Desoxycorticosterone acetate was given twice daily intramuscularly with intravenous injections twice daily of 5 per cent dextrose in physiologic solution of sodium chloride before and after operation.						Control Group: Twice daily 5 per cent dextrose in physiologic solution of sodium chloride was given intravenously before and after operation.					
		Administration of Desoxycorticosterone Acetate						Intravenous Administration of Dextrose-Saline Solution			
Age	Sex	Days Pre-operative	Days Post-operative	Days in Hospital	Complications	Age	Sex	Days Pre-operative	Days Post-operative	Days in Hospital	Complications
					Cholecystenterostomy for Carcinoma of the Pancreas						
67	M*	2	10	18	None	58	F*	2	3	18	None
48	M*	2	13	15	None	60	F*	2	3	5‡	Pulmonary embolism
					Excision of Retroperitoneal Sarcoma						
72	M*	2	11	22	None	37	F*	1	2	15	None
					Thoracotomy for Excision of Sarcoma of the Thoracic Cavity						
55	F*	3	3	9‡	Pulmonary embolism	16	M*	1	1	2‡	Cardiac decompensation
					Previous Cholecystostomy for Acute Pancreatitis, Secondary Cholecystectomy and Choledochostomy with T Tube for Lithiasis						
53	F*	1	16	22	None	46	F*	2	3	21	None
					Thoracoplasty for Pulmonary Tuberculosis						
56	M*	1	15	30	None	32	M*	1	2	28	None
					Nephrectomy for Carcinoma						
62	M*	2	12	15	None	48	F*	1	2	16	None
					Anterior Gastrojejunostomy for Inoperable Carcinoma with Obstruction						
70	F†	1	13	19	None	71	F†	1	3	15	None
					Laparotomy for Carcinoma of the Stomach (Found Inoperable at Operation)						
62	F*	1	14	17	None	66	M*	1	3	15‡	Pulmonary embolism
					Ileosigmoidostomy for Carcinoma						
70	F*	3	14	24	None	61	F*	1	3	26	None
					Colostomy for Carcinoma						
58	M*	1	13	28	None	42	F*	1	3	31	None
50	M*	2	13	27	None	40	M*	2	2	21	None
54	F*	2	14	27	Pneumonia in the right lower lobe	60	F*	2	1	18	None
					Obstructive Resection for Carcinoma						
59	F*	1	14	46	None	68	M*	1	3	38	None
					Splenectomy						
46	F*	3	13	21	None	64	F*	1	3	22	None
					One Stage Resection for Regional Enteritis						
53	F*	1	13	29	None	62	F*	1	3	4‡	Bilateral bronchopneumonia
37	M§	1	13	26	Fecal fistula	29	F§	1	3	35	Fecal fistula
30	M*	3	7	10‡	Pneumonia	18	F*	1	3	31	None
23	M§	1	12	53	None	26	M§	1	3	17	None
25	M	1	13	18	None	20	F	1	3	21	None

* Fair condition.
† Poor condition.
‡ Patient died.
§ Exteriorization of the anastomosis.

TABLE 8.—*Data on Treated and Control Patients Who Were in Some Degree of Shock at the Time of Operation*

Treated Group					Control Group				
Five cubic centimeters of adrenal cortical extract was given four times a day for two days; then 1 ampule of desoxycorticosterone acetate twice daily for four days and daily for eight days. Five per cent dextrose in physiologic solution of sodium chloride also was given intravenously.					Five per cent dextrose in physiologic solution of sodium chloride only was given.				
Age	Sex	Days of Post-operative Treatment	Days in Hospital	Complications	Age	Sex	Days of Post-operative Treatment	Days in Hospital	Complications
Cholecystectomy and Choledochostomy with T Tube Drainage and Drainage of the Pancreas for Acute Pancreatitis									
31	F*	14	25	None	42	M*	5	25	None
53	F†	14	18	None	40	M†	4	23	None
58	M†	3	3‡	Peritonitis	63	F†	3	19	None
Purse String Suture for Acute Perforated Gastroduodenal Ulcer									
47	M*	14	15	None	25	M*	3	18	None
50	M†	14	18	None	77	M†	3	16	None
Amputation of Leg (Midthigh)									
8	M†§	14	72	None	69	M†‖	2	45	None

* Fair condition.
† Poor condition.
‡ Patient died.
§ Patient had compound fracture of both legs with gangrene of the right leg.
‖ Debilitated patient with diabetes and gangrene of the right leg.

Twelve of the 200 patients (6 treated and 6 untreated) had conditions acute in nature and were considered in shock at the time of operation. Four had perforated pyloric ulcers; 6 had acute hemorrhagic pancreatitis, and 2 had amputations of the lower extremity—the one, a young boy of 8 years who suffered from severe shock following compound fracture of both legs, and the other, an old debilitated patient with diabetes and gangrene. The treated patients with acute conditions were given 5 cc. of adrenal cortical extract intramuscularly every six hours for the first forty-eight and then 5 mg. of desoxycorticosterone acetate twice daily for four days and once daily subsequently for ten to fourteen days. All received 1,000 cc. of 5 per cent dextrose in physiologic solution of sodium chloride twice daily for the first four days. The other 94 patients in the treated group (there was ample opportunity to prepare them preoperatively since they were being operated on for chronic lesions) all were given 5 mg. of desoxycorticosterone acetate twice daily for anywhere from one to four days before operation and the same dose twice daily for the first four days postoperatively; after this only one injection a day was given up to the fourteenth day after operation. All of them received intravenous injections of 1,000 cc. of 5 per cent dextrose and saline solution twice a day before operation and for the first four days after operation. The 94 control patients were treated in exactly the same manner except that they received no desoxycorticosterone acetate or adrenal cortical extract. Transfusions and supplementary vitamin therapy were given to patients in both groups whenever it was believed the indication warranted it.

RESULTS

The effect of the therapy on the operation and the convalescence and the result in the control cases are given in tables 2 to 8.

COMMENT

From a study of the 200 cases selected for this experiment, it can be seen that the value of any addition to the therapy ordinarily employed should be reflected in the mortality rate. If desoxycorticosterone acetate could do anything to prevent death, these cases would offer it a fine opportunity to demonstrate its usefulness. Among the 100 treated patients, there was a mortality rate of 11 per cent, and among the control patients, there was a mortality rate of 9 per cent. Even if reversed, this difference of percentages has absolutely no significance according to the method of calculating the significance of differences in percentages suggested by Fisher.[20] Previous workers in this field have, however, attached significance to the results obtained by the use of adrenal cortical extract. Wilson, MacGregor and Stewart [12a] expressed the opinion that adrenal cortical extract may have a favorable influence in the treatment of shock from burns and scalds. They gave the protocols of 13 cases, in only 3 of which adrenal cortical extract was given. Two of the 3 patients recovered, 1 supposedly with a dramatic effect as a

20. Fisher, R. A.: Statistical Methods for Research Workers, ed. 6, Edinburgh, Oliver & Boyd, 1936, p. 47.

result of the use of extract of adrenal cortex. The authors mentioned in the text that their personal experience was limited to 3 additional cases, in 2 of which adrenal cortical extract was without obvious action. Their impressions, therefore, were gained from 6 cases. Since 3 of the patients died, it was obviously of no value in this small group of cases. Reed [1c] gave adrenal cortical extract to a series of over 50 operative patients. He reported 8 cases in detail. Two patients were operated on for pelvic inflammatory disease; 2, for acute appendicitis; 1, for chronic appendicitis; 1, for cholecystitis; 1, for ectopic pregnancy, and 1, for thyroid adenoma. Without any controls, Reed gathered the clinical impression that the use of adrenal cortical extract either prevented shock or, when shock occurred, was of definite value in helping the patient combat it. Perla [1b] gave desoxycorticosterone acetate and solution of sodium chloride to 12 patients who were considered poor risks; their cases were reported because no shock developed in them and they all recovered. Discussing experiences at a casualty-clearing station in a small military hospital where the major problem was the treatment of 500 of the more seriously wounded evacuated from Flanders, Brown, Dennison, Ross and Divine [18a] described the routine treatment which they gave in 20 cases of extensive second and third degree burns. All of their patients exhibited secondary shock or toxemia on admission, and some had suffered from immersion in the sea. Besides their routine burn treatment, they used desoxycorticosterone acetate also. They felt that desoxycorticosterone acetate proved its value in many of these cases. Among the 20 patients treated there was a mortality rate of 25 per cent. However, there were no control observations, and the number of observations was limited to 20 as has already been mentioned. Besser [1d] attempted a controlled experiment and reported on the value of desoxycorticosterone acetate in the prevention of operative shock in 72 cases. He pointed out the difficulty of determining the value of a therapeutic measure in the prevention of shock associated with operative procedures, and he arbitrarily used a blood pressure of 80 systolic and 60 diastolic as the level below which the onset of shock was indicated. He pointed out also that the use of methods to determine hemoconcentration was not satisfactory under the conditions of the experiment, since many other circumstances besides shock itself could contribute to changes in hemoconcentration. As controls, he used 68 untreated patients, and he concluded (clinical impression) that desoxycorticosterone was of little value in preventing shock. Unfortunately, no information was given regarding the mortality rate in the treated and the untreated group.

If it can be assumed that all deaths in the treated and control groups in our experiment were due to shock alone, then desoxycorticosterone acetate manifestly had no value in preventing shock since there were more

deaths in the treated series. To show that the treatment had any value, it would be necessary to find a lower mortality rate in the treated than in the control group. To be statistically significant, the difference in mortality rate, it can be shown, would have to be greater than 6 per cent. By this is meant that if the control group mortality rate of 100 patients is 9 per cent, then in the treated group of 100 patients the mortality rate must be less than 3 per cent to establish the probability that the difference between the two was other than an accidental occurrence.

It is likely that other factors besides shock contributed to the deaths in both groups. It therefore becomes evident that the mortality rate in the treated group would have to be even less than 3 per cent to be significant, if the trial is limited to 200 cases. Since, however, there was no reduction in the mortality rate in the treated group, it may be concluded that there is no evidence in this experiment that desoxycorticosterone acetate can prevent or favorably influence postoperative shock as reflected by the mortality rate. It seems also that enthusiastic reports of its value in other instances of its use in human beings are not supported by data.

SUMMARY

Two hundred patients operated on for conditions such that shock might reasonably be expected to develop during or after the operation were studied in this experiment. One hundred alternately chosen were treated with desoxycorticosterone acetate and parenteral solution of sodium chloride. The mortality rate in the treated and control groups was used as the criterion of the effectiveness of the therapy, the term "shock" being assumed to denote an irreversible state of circulatory failure.

There was no evidence that the therapy prevented or favorably influenced shock.

PRACTICAL METHOD OF PREDICTING THE GROWTH OF THE FEMUR AND TIBIA IN THE CHILD

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Inequality in the length of legs is a problem which is fundamentally important to the orthopedic surgeon. Before the development of our method of leg lengthening,[1] the standard treatment prescribed for patients with shortening of one of the lower extremities was the application of a lift to the sole of the shoe.[2] The success of the method employed by us aroused new interest on the part of orthopedic surgeons in many clinics throughout the country. Later, the original technic was modified in the hope that the operation could be simplified and freed from complications.[3] Despite these efforts, the operation remains today one of considerable magnitude and one to be performed only in a selected group of cases. It should never be attempted by the inexperienced surgeon who lacks detailed and anatomic knowledge of every step of the operation and the postoperative care.

After considerable experience with the procedures for lengthening the femur and lengthening the tibia and the fibula, we have reached the opinion that while the main purpose of our method is of limited value, a number of valuable by-products have been developed. The approaches

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Read before the American Academy of Orthopaedic Surgeons, New Orleans, Jan. 15, 1941.

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This work was supported by the Florence Hellman Ehrman Donation for Crippled Children and the Christine Breon Fund for Medical Research.

1. This method was developed at the Shriners' Hospital for Crippled Children, St. Louis, by Drs. L. C. Abbott and C. H. Crego Jr. and at the University of California Medical School by Drs. L. C. Abbott and John B. deC. M. Saunders.

2. Abbott, L. C.: The Operative Lengthening of the Tibia and Fibula, J. Bone & Joint Surg. **9**:128 (Jan.) 1927.

3. Abbott, L. C., and Saunders, J. B. deC. M.: The Operative Lengthening of the Tibia and Fibula: A Preliminary Report on the Further Development of the Principles and the Technique, Ann. Surg. **110**:961 (Dec.) 1939.

which have been devised as a result of the many anatomic dissections are useful in other operations on the lower extremities. Furthermore, the dissections have accurately shown the points of fixation by fascia of the nerves of the extremity. For example, the common peroneal and posterior tibial nerves are fixed respectively at the neck of the fibula and the upper border of the soleus muscle. Freeing these nerves from their points of fixation together with flexion of the knee produces sufficient slackening to permit lengthening of the tibia and the fibula 1½ inches (3.8 cm.) without undue tension on the substances of the nerves. This information is useful to the surgeon in suturing the nerves when there has been a considerable loss of substance. The apparatus which has been devised with a two, three and four pin fixation for the control of the fragments after osteotomy has led to the use of similar traction appliances for the treatment of complicated fractures. In some fractures, the use of these appliances has obviated the necessity for open reduction. Experience with leg-lengthening procedures gives further knowledge regarding the formation of callus and the effects of stress and strain on early formation of bone.

As an alternative procedure to lengthening the short leg, shortening of the sound leg is now commonly employed. It is the most accurate method for the equalization of the length of the legs. In considering its use, however, it is well to remember that in the growing child there may be a number of factors producing discrepancy in length which require a period of observation and study. Further, the rate of growth of the shortened leg may be altered considerably by changes in the circulation as a result of operative procedures or continued activity of disease with the involvement of epiphysial cartilage plates. In our opinion, therefore, the operation of leg shortening should be reserved for use in cases in which growth has been completed.

The operation of leg shortening has been performed with many types of osteotomy. If the operation is ever indicated in young children, simple transverse division of the bone, overlapping of the fragments to the desired amount and then fixation by horizontal pins seems to be satisfactory.[4] In older children and adults, a more carefully planned osteotomy with mortising of the fragments is essential. The underlying principles are the same in any of the operative procedures, namely, restoration of alinement and complete fixation of the fragments until union takes place.

4. White, J. W., and Warner, W. P.: Experiences with Metaphyseal Growth Arrests, South. M. J. **31**:411 (April) 1938.

The operation has been performed in the upper, middle and lower thirds of the femur. We have had success with the use of all three sites, but union has taken place with greater rapidity when the osteotomy has been performed through cancellous bone at either the upper or the lower third. The least disturbance to the function of the quadriceps muscle group and to the knee joint occurs when osteotomy is done through the upper third. A special type of osteotomy together with a description of the anatomic approach which we have used in this region will be discussed in a later article.

In growing children, the most useful method for equalization of leg length is the epiphysial arrest advocated by Phemister.[5] This operation is simple, its only drawback being the permanent shortening of stature. This procedure used alone or with operations for lengthening of the leg demands an accurate method of estimating the future rate of growth, the ultimate length of the extremities and the final height.

In this paper we shall describe a method for the prediction of future growth of the femur and the tibia which we believe to be the most reliable of all methods of which we have knowledge. Before describing it in detail, we shall review in brief the work of others with relation to this problem.

The studies of Phemister and Hatcher have been of great importance in emphasizing the value of epiphysial arrest in the treatment of inequality in the leg length of growing children. To make this operation of practical value, they devised a method of determining the average growth of the lower limbs at various ages. These authors used Baldwin's data, which represented average measurements for the standing and the sitting height of a large group of children at various ages. The growth in the length of the legs at each age was determined by subtraction of the average leg length at each age from the average length of the legs at full growth.[6] Digby's figures for the percentage of growth from the individual epiphyses of the femur and the tibia were converted into percentages of growth for the entire lower extremity.[7] These percentages were then multiplied by the expected growth of the leg in order to give the exact amount of growth contributed by each epiphysis. An attempt was made to individualize the predictions of growth by using the stature and the leg length of the parents.

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5. Phemister, D. B.: Operative Arrestment of Longitudinal Growth of Bones in the Treatment of Deformities, J. Bone & Joint Surg. **15**:1 (Jan.) 1933.

6. Baldwin, B. T.: Physical Growth of Children from Birth to Maturity, Studies in Child Welfare, Iowa City, University of Iowa, 1921, vol. 1, no. 1.

7. Digby, K. H.: The Measurement of Diaphyseal Growth in Proximal and Distal Directions, J. Anat. & Physiol. **50**:187, 1915-1916.

We believe, however, that there are five valid objections to this method of estimating the possible growth from the individual epiphyses of the femur and the tibia. The same criticisms apply to similar methods used by Wilson and Thompson [8] and White.[4]

1. Average figures for the length of legs cannot be applied because of the wide variations in the final leg length of individual children. Meredith's figures for leg length at completed growth show that in boys the measurements ranged from 27.8 to 37.3 inches (70.61 to 94.74 cm.), a difference of 9½ inches (24.13 cm.) (fig. 1). In girls, the range was from 26.6 to 34.1 inches (67.56 to 86.61 cm.), a variation of 7½ inches

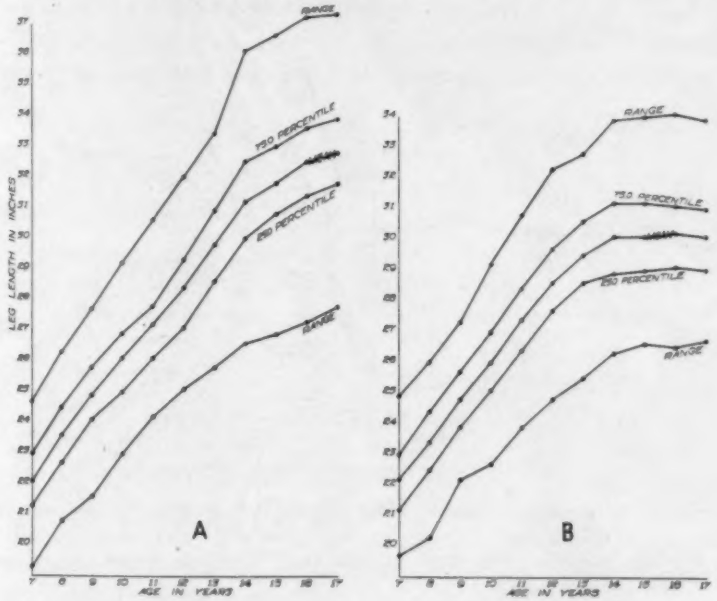

Fig. 1.—Leg lengths as drawn from data of Meredith, i. e., stature minus stem length. *A*, boys; *B*, girls.

(19.05 cm.).[9] In addition, Bach [10] found that in adults of various heights there is so much disparity in the proportions of the length of

8. Wilson, P. D., and Thompson, T. C.: A Clinical Consideration of the Methods of Equalizing Leg Length, Ann. Surg. **110**:992 (Dec.) 1939.

9. Meredith, H. B.: Length of Head and Neck, Trunk and Lower Extremities on Iowa City Children Aged Seven to Seventeen Years, Child Development **10**: 129 (June) 1939.

10. Bach: Veränderungen der Oberschenkellänge und Unterschenkellänge mit steigender Körpergrösse, in Martin, R.: Lehrbuch der Anthropologie, ed. 2, Jena, Gustav Fischer, 1928, vol. 1, pp. 416-417.

the limbs to the total stature, that many persons of medium height may have legs as long as taller persons (fig. 2).

2. Leg length is an unsatisfactory measurement for several reasons. It is usually obtained by subtracting the sitting height from the standing height and for that reason includes structures other than the femur and the tibia. From this measurement, it is not possible to study the growth of the normal bones and, even more important, to determine the actual mechanism producing abnormal growth in any given case. On the other hand, teleroentgenograms taken with the tube at a distance of 6 feet (183 cm.) give a permanent record of the length of the femur and the tibia

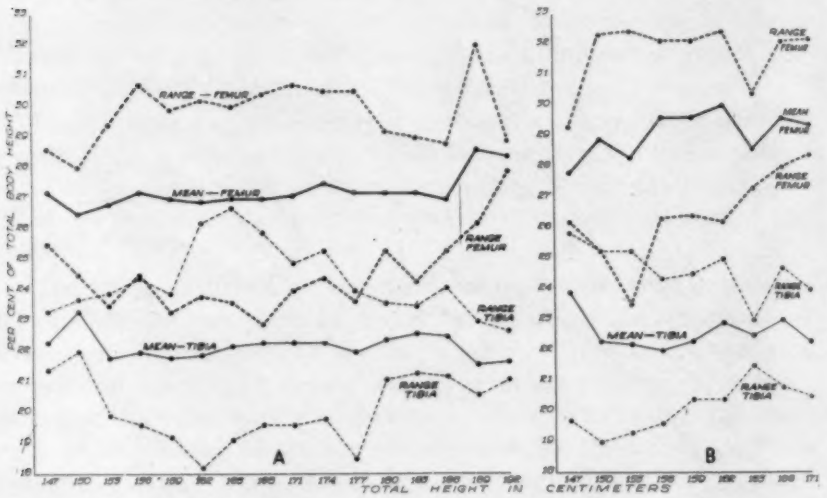

Fig. 2.—Leg length as percentage of total body height as drawn from data of Bach. *A*, men; *B*, women.

with only a small degree of distortion. This distortion is almost constant and may therefore be virtually disregarded in most instances.

Another method, slit scanography, devised by Millwee,[11] is even more accurate. Recently, we have been using a modification of this method which is now in process of further development. The tube port is covered by a lead mask with a transverse slit 2 mm. wide. During a lengthened exposure, the tube is slowly moved the length of the bone to be measured at a rate of about 36 inches (91 cm.) per ten seconds This results in films of good quality with the exact lengths of the bones. The distance of the tube from the limb may be as short as desired.

11. Millwee, R. H.: Slit Scanography, Radiology **28**:483 (April) 1937.

3. There is no allowance for the frequent variations in the sexual and the skeletal development of children of the same age. This, as will be shown later, may lead to serious errors in the prediction of the future growth of a child.

4. The use of the parents' measurements is not reliable in determining the future growth of the child. Baldwin [6] and Wallis [12] have shown in their studies that calculations of the final growth of the child based on its measurements with relation to those of its group are more accurate than those based on the measurements of its parents. It seems obvious that with parents of varying height, it would be impossible to guess which parent the child might resemble in final stature.

5. Digby's figures, as used by Phemister and Wilson, presuppose that the femur and the tibia grow at the same relative rate during the

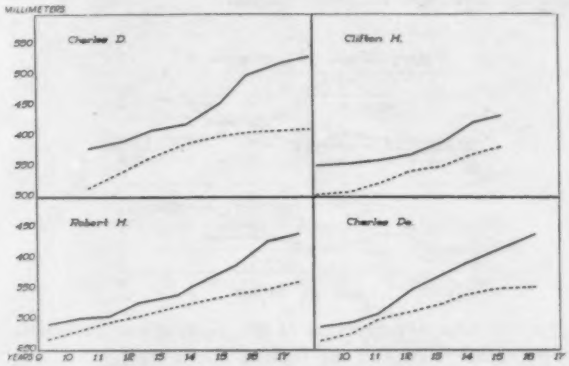

Fig. 3.—Growth curves of the upper and the lower parts of the leg as drawn from data of Davenport. The solid line represents the upper part of the leg, and the broken line, the lower part. All the patients were white boys except Clifton H., who was a mixture of Negro and white.

entire period of growth. This, however, is not true, as was shown by Schultz,[13] Schwerz [14] and Davenport.[15] Davenport demonstrated that

12. Wallis, R. S.: How Children Grow: An Anthropometric Study of Private School Children from Two to Eight Years of Age, Studies in Child Welfare, Iowa City, University of Iowa, 1931, vol. 5, no. 1.

13. Schultz, A. H.: Fetal Growth of Man and Other Primates, Quart. Rev. Biol. **1**:465 (Oct.) 1926.

14. Schwerz: Schaffhauser Kinder, in Martin, R.: Lehrbuch der Anthropologie, ed. 2, Jena, Gustav Fischer, 1928, p. 414.

15. Davenport, C. B.: The Crural Index, Am. J. Phys. Anthropol. **17**:333 (Jan.-March) 1933.

there is a change in the relative rates of growth of these bones in boys (fig. 3). The femur, longer than the tibia at birth, grows slowly in the juvenile period. At the age of 11 or 12 years, just before puberty, it begins to grow more rapidly. In contrast, the tibia grows uniformly, though at a faster rate than the femur during the juvenile period until about the age of 13 or 14, when its growth is damped off just at the time the femur is beginning to grow more rapidly. Thus, the tibia obtains its final growth before the femur. The results of the work of Schwerz (fig. 4) agreed fairly well with those of Davenport, though the study was based on average measurements, which tend to mask the findings shown by a study of an individual case like Davenport's. Hatcher's curves of growth for the femur and the tibia show no change in the relative rates of growth of these bones.[16] However, these curves also are based on average measurements.

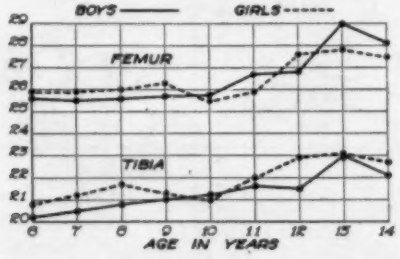

Fig. 4.—Femur and tibia as percentage of stature as drawn from data of Schwerz. The solid line represents boys, and the broken line, girls.

METHOD

From an extensive review of the anthropologic literature on the growth of children, we have developed a method which to a great extent overcomes the objections just mentioned. While we believe that it is more accurate than any now in use, we realize that it may be improved on as more detailed data on the growth of children is obtained. This method is based on two findings: 1. The final stature of a child may be predicted accurately by the use of the percentile method. This accuracy is increased if the bone maturation age of the child is considered. 2. The relative proportions of the length of the femur and the tibia to stature in a person are maintained with only small age variations throughout the adolescent period. Therefore, it is a matter of simple arithmetic to predict the final length of the femur and the tibia in any child by taking the present proportions of these bones to stature, adding small changes according to age and multiplying these proportions by the predicted final height.

16. Hatcher: Growth Increment Curve for the Femur and Tibia, in Campbell, W. C.: Operative Orthopedics, St. Louis, C. V. Mosby Company, 1939, p. 954.

Our method of determining the expected growth of the normal femur and tibia is as follows:

1. The child's height is measured as it stands on the normal leg with the pelvis level.[17]

2. The age is recorded in years and months. This is checked against the skeletal maturation age obtained from Todd's Atlas of Skeletal Maturation

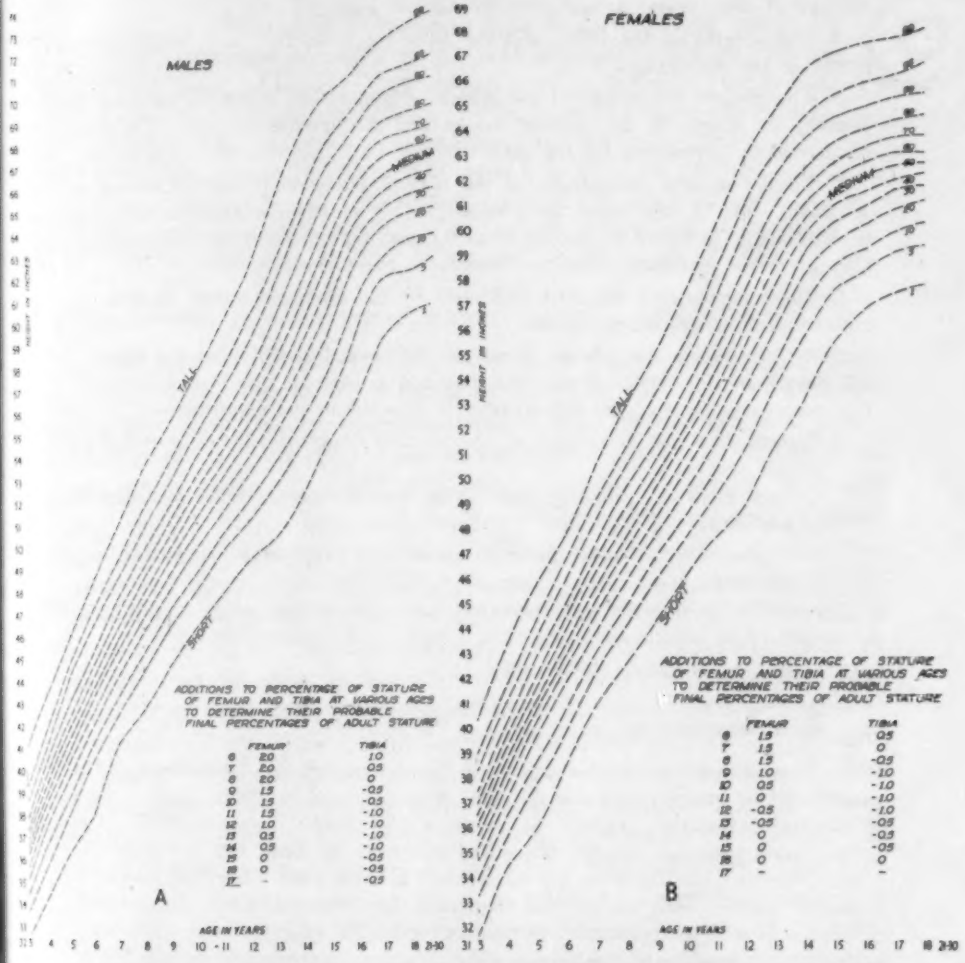

Fig. 5.—Curves of percentile distribution of height constructed from the tables for percentile distribution of stature given by the White House Conference on Child Health and Protection in 1932. The subtables included in the charts were compiled from different data.

17. Measurement of the total height is taken with the patient standing on the normal leg. Blocks are placed under the short leg until the pelvis is level. The buttocks, the shoulders and the head should touch the wall.

(Hand).[18] If the skeletal maturation is more than six months advanced or retarded from the chronologic age, the skeletal age should be substituted for the chronologic age in all further calculations.

3. From the sex, the height and the corrected age, the person is placed in his or her percentile position of the percentile chart (fig. 5).[19] By following up the chart between the parallel percentile curves to the completion of growth, the expected final stature of the person is obtained. In boys, growth is complete at the age of 18½ years; in girls, at the age of 16½.

4. The lengths of the femur and the tibia are measured from teleroentgenograms or slit scanograms.[20]

5. The present percentage of the normal femur to the stature is obtained by dividing its length by the present height and multiplying by 100. The same calculation is carried out for the tibia.

6. To the present percentages of the normal femur and tibia to stature, as calculated under 5, are added the amounts, either positive or negative (as given in the subtable in figure 5), according to the sex, the corrected age and the bone. This gives the estimated adult percentages of these bones to stature.

7. These percentages are then multiplied by the predicted stature to give the expected final length of each bone.

8. By subtracting the present length of the normal femur from the expected final length of the normal femur, the expected growth of this bone is obtained. The expected growth of the normal tibia is obtained in the same manner.

9. Growth from the distal part of the femur = expected femoral growth × 70 per cent

Growth from the proximal part of the tibia = expected tibial growth × 55 per cent

Growth from the distal part of the tibia = expected tibial growth × 45 per cent

The following example will serve to clarify the various steps in predicting the growth of the normal femur and tibia. Suppose the patient to be a girl.

1. Height = 53 inches (160.02 cm.)

2. Age = 9 years

Bone maturation age = 10 years.

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18. The skeletal maturation age may be determined by comparison of an anteroposterior roentgenogram of the hand with standards in Todd, T. W.: Atlas of Skeletal Maturation (Hand), St. Louis, C. V. Mosby Company, 1937. The skeletal maturation age may be determined also from the knee, but, unfortunately, Todd's standards for the knee are not printed in atlas form. For this reason, it is simpler to determine the skeletal maturation age from the hand.

19. The curves of percentile distribution of height (fig. 5) were constructed by us from the tables for percentile distribution of stature given by the White House Conference on Child Health and Protection in 1932.[21]

20. The lengths of the femur and the tibia are to be determined from roentgenograms of the femur and the tibia taken at a distance of 6 feet (183 cm.), the tube to be centered in the approximate middle of each bone or from scanograms. From these films the measurements are made as follows: femur, a straight line from the tip of the femoral head to the medial lip of the internal femoral condyle at the joint line; tibia, a straight line from the medial lip of the internal tibial condyle at the joint line to the tip of the internal malleolus.

3. The expected total stature = 64 inches (162.56 cm.)
4. Length of femur = 14.8 inches (35.56 cm.)
   Length of tibia = 12.5 inches (31.75 cm.)
5. Femoral percentage of stature = $\frac{14.8 \text{ inches}}{53 \text{ inches}} \times 100 = 28$ per cent
   Tibial percentage of stature = $\frac{12.5 \text{ inches}}{53 \text{ inches}} \times 100 = 23.5$ per cent
6. Femoral percentage of adult stature = 28 + 0.5 = 28.5 per cent
   Tibial percentage of adult stature = 23.5 + (-1.0) = 22.5 per cent
7. Final length of femur = 28.5 per cent × 64 = 18.2 inches (46.23 cm.)
   Final length of tibia = 22.5 per cent × 64 = 14.4 inches (36.58 cm.)
8. Expected growth of femur = 18.2 — 14.8 = 3.4 inches (8.64 cm.)
   Expected growth of tibia = 14.4 — 12.5 = 1.9 inches (4.83 cm.)
9. Growth distal femur = 3.4 × 70 per cent = 2.4 inches (6.1 cm.)
   Growth proximal tibia = 1.9 × 55 per cent = 1.05 inches (2.67 cm.)
   Growth distal tibia = 1.9 × 45 per cent = 0.85 inches (2.16 cm.)

PREDICTION OF THE FINAL HEIGHT OF THE INDIVIDUAL CHILD

The accuracy of our predictions rests on the exactness with which height may be predicted by the percentile method. This method has long been used because numerous studies have shown that in a group of children, a given child tends to maintain his rank in stature from one age to another. In 1921, Baldwin [6] followed the growth in height of a small series of boys and girls representing similar stock. When the individual curves were plotted, he found that for each sex the curves of growth assumed a railroad appearance, each child maintaining his or her relative position from the ages of 6 to 17 years. There was a crossing of curves because girls have an earlier acceleration and an earlier cessation of growth than boys. From his data, Baldwin concluded that the height at the age of 15 or 16 years could be predicted within 3 or 4 cm. if the height were known at the age of 9 or 10 years. When Baldwin's children were plotted in a percentile manner, they stayed rather closely within their percentile range. In 1922, Porter found that the chances were 3 to 1 that no boy would vary as much as 14 percentile grades between the ages of 6 and 13 years. We have constructed the curves we use from the tables for percentile distribution of stature published in 1932 by the Committee on Growth and Development of the White House Conference on Child Health and Protection (fig. 5).[21] The 1 percentile grade is the stature of the shortest 1 per

21. Growth and Development of the Child: I. General Considerations, Report of the Committee on Growth and Development, Section 1, Medical Service, White House Conference on Child Health and Protection, New York, Century Company, 1932, pp. 93-108; Percentile tables, pp. 98-101; II. Anatomy and Physiology, ibid., 1933, pp. 55-74; IV. Appraisement of the Child, ibid., 1932, pp. 258-278.

cent at each age; the 50 percentile grade, the stature of the persons in the middle group at each age; the 99 percentile grade, the stature of the tallest 1 per cent, and so on. To determine whether height could be predicted accurately enough for our purposes by the use of these curves, we reviewed the measurements of a group of children who had been followed to full growth. These children represented an average group of varying nationalities. The state of health varied, but none of the children was severely ill. A prediction of final height was made from each measurement taken during the growth period by following up between the parallel curves. These predictions were then compared to the actual final stature. In this manner, errors in the prediction of height for each age were readily found. Unfortunately, the children were not measured at sufficiently regular intervals to allow the calculations of the average error in the prediction of final height in each case.

In 33 girls (tables 1 and 2), the largest errors in the prediction of height in 75 per cent of the cases were less than 1.8 inches (4.58 cm.). In 12 boys (table 3), the largest errors in 75 per cent of the cases were less than 2½ inches (6.35 cm.). It must be remembered that these figures were based on the selection of the greatest discrepancy in each case. In all of the cases most of the errors were smaller. When we averaged our data, admittedly incomplete, the average error in the prediction of total stature was 1 inch (2.5 cm.), and in 90 per cent of the cases, the average error was under 2 inches (5.08 cm.). As the tibia and the femur each compose only about one fourth of the total stature, the error in the prediction of the length of these two bones would be one fourth of this amount. There is evidence that even these errors may be reduced by substitution of the bone maturation age for the chronologic age. Meredith found that there is often considerable variation in the percentile standing of children after the period of adolescence.[22] This is caused by differences in the degree of sexual maturation. For example, given 2 children of the same sex, height and actual age, the one with the most advanced sexual development will always become the shorter adult.[22a] Todd showed clearly that sexual maturation is closely correlated with skeletal maturation. He found that regardless of their chronologic age, girls began menstruation at an average skeletal maturation of 13½ to 14 years.[23] This age is the average age of menstruation for many large groups of girls.

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22. Meredith, H. B.: Stature of Massachusetts Children of North European and Italian Ancestry, Am. J. Phys. Anthropol. **24**:301 (Jan.-March) 1939.

22a. Wilson and Thompson.[8] Meredith.[22]

23. Todd, T. W.: Growth and Development of the Skeleton, in Preliminary Report of the Committee on Growth and Development, White House Conference on Child Health and Protection, 1930, Sect. 1, Medical Service, New York, Century Company, 1930, p. C1. The Anatomical Features of Epiphyseal Union, Child Development **1**:186 (Sept.) 1930.

TABLE 1.—*Errors in Height Prediction of Girls with Theoretic Correction of Chronologic Age of Menstruation to Thirteen and a Half Years*

TABLE 1.—*Errors in Height Prediction of Girls with Theoretic Correction of Chronologic Age of Menstruation to Thirteen and a Half Years*

Patient	Final Age	5 Yr.	6 Yr.*	7 Yr.	8 Yr.	9 Yr.	10 Yr.	11 Yr.	12 Yr.	13 Yr.	14 Yr.	15 Yr.	Maximum Error	Age at Which Menstruation Began	Comment
1	18 yr., 9 mo.	..	.....	.....	.....	+1.8 −1.0	+2.2 −0.3	.....	+2.8 +0.6	+2.4 +0.7	+2.0 +0.4	.....	+2.8 −1.0	12 yr.	
2	17 yr., 4 mo.	..	.....	.....	.....	.....	+4.3 +2.0	+5.2 +2.2	.....	+4.2 +1.5	.....	+1.8 +1.3	+5.2 +2.2	12 yr.	Latin
3	18 yr.	..	+2.1 −2.4	+1.9 −1.6	+1.9 −1.0	+2.1 −0.9	+2.5 −0.8	+2.7 −0.6	+2.5 0	+1.7 −0.3	+1.0 −0.4	+1.1 +0.1	+2.7 −2.4	12 yr.	
4	17 yr.	..	.....	.....	.....	+1.0 −1.5	0 −1.8	+1.8 +0.1	+1.8 +0.2	+1.5 +0.2	+1.3 +0.6	.....	+1.8 −1.8	12 yr., 5 mo.	
5	16 yr., 10 mo.	..	.....	.....	+3.5 +1.4	.....	.....	.....	+2.0 0	+2.3 +1.1	+1.9 +1.2	+1.3 +1.0	+3.5 +1.4	12 yr., 7 mo.	
6	19 yr.	..	.....	.....	.....	+0.5 −1.0	+0.7 −0.8	+1.3 −0.3	.....	+2.0 +1.2	.....	+0.7 +0.3	+2.0 +1.2	12 yr., 10 mo.	
7	19 yr.	..	.....	.....	.....	.....	.....	.....	+1.2 +0.5	.....	+0.7 −0.1	+0.5 +0.3	+1.2 +0.5	12 yr., 11 mo.	Rheumatic fever at 11 years of age
8	17 yr., 7 mo.	..	.....	.....	.....	.....	−0.6 −1.5	+0.6 −0.5	.....	.....	+0.6 +0.3	+0.6 +0.3	±0.6 −1.5	13 yr.	
9	17 yr.	..	.....	.....	−1.1 −2.0	.....	.....	.....	.....	+0.8 −0.2	.....	+0.8 +0.2	−1.1 −2.0	13 yr.	Congenital syphilis
10	16 yr., 9 mo.	..	.....	.....	.....	.....	.....	−1.0 0	0 +0.8	−0.5 +0.1	+0.4 +1.0	+1.0 +1.3	±1.0 +1.3	14 yr.	
11	17 yr., 8 mo.	..	.....	.....	.....	.....	.....	−0.5 +1.0	−1.6 −0.9	.....	.....	−0.8 −0.3	−1.6 +1.0	14 yr.	
12	17 yr.	..	−0.2 +1.5	+0.2 +1.5	+0.2 +1.5	0 +1.5	−0.2 +0.8	−1.7 +0.4	−1.8 0	−1.8 −0.5	−1.1 0	−0.7 0	−1.8 +1.5	14 yr., 3 mo.	
13	17 yr., 11 mo.	..	.....	−0.9 +1.4	.....	.....	.....	.....	−0.4 +0.8	−0.8 0	.....	0 +0.2	−0.9 +1.4	14 yr., 5 mo.	
14	16 yr., 9 mo.	..	.....	.....	−2.4 0	−1.2 +0.8	−1.2 +0.8	−1.2 +0.7	−2.4 0	−1.5 −0.1	−1.3 +0.8	−0.5 +0.8	−2.4 +0.8	14 yr., 7 mo.	
15	17 yr., 2 mo.	..	.....	−2.7 +1.2	.....	.....	.....	.....	−3.0 −0.3	.....	−1.6 +0.8	−1.0 +1.2	−3.0 +1.2	15 yr.	
16	18 yr., 1 mo.	..	.....	.....	.....	.....	.....	.....	.....	−2.1 +0.5	−1.5 +1.3	.....	−2.1 +1.3	15 yr., 3 mo.	
17	18 yr., 7 mo.	..	.....	.....	.....	+1.0	+2.0	.....	.....	+1.0	.....	.....	+2.0	13 yr., 8 mo.	

Errors in Prediction of Height (Uncorrected)

Average maximum error	2.18 in. (5.53 cm.)
50 per cent under	2.0 in. (5.08 cm.)
75 per cent under	2.8 in. (7.02 cm.)
90 per cent under	3.5 in. (8.89 cm.)
Range	5.2 in. (5.08 cm.)

Errors in Prediction of Height with Theoretic Correction of Chronologic Age of Menstruation to Thirteen and a Half Years

Average maximum error	1.5 in. (3.81 cm.)
50 per cent under	1.4 in. (3.56 cm.)
75 per cent under	2.0 in. (5.08 cm.)
90 per cent under	2.2 in. (5.59 cm.)
Range	2.4 in. (6.10 cm.)

* Lower figures represent corrections.

TABLE 2.—*Errors in Height Prediction of Girls for Whom the Age at Which Menstruation Began Was Not Known*

Patient	Final Age	5 Yr.	6 Yr.	7 Yr.	8 Yr.	9 Yr.	10 Yr.	11 Yr.	12 Yr.	13 Yr.	14 Yr.	15 Yr.	Maximum Error	Comment
1	18 yr., 4 mo.	+2.5	+2.0	.....	+1.5	+1.5	.....	+1.3	+1.2	.....	.....	+0.1	+2.5	Congenital heart disease
2	17 yr., 5 mo.	0	.....	.....	0	+0.6	+1.2	+1.0	+1.0	.....	+0.5	+0.3	+1.2	Rheumatic heart disease
3	20 yr., 2 mo.	.....	−1.0	.....	.....	.....	.....	−0.5	.....	+0.3	.....	0	−1.0	
4	17 yr., 8 mo.	.....	.....	+0.3	.....	.....	.....	−0.8	−0.8	.....	−1.0	.....	−1.0	
5	16 yr., 8 mo.	.....	.....	−1.5	.....	−1.1	−0.8	.....	−0.6	−1.2	−0.6	−0.2	−1.5	
6	17 yr., 4 mo.	.....	.....	+0.4	+0.3	+0.3	+0.7	−0.7	−1.0	−1.2	.....	−1.0	−1.2	
7	16 yr., 11 mo.	.....	.....	.....	−0.6	+0.8	.....	+0.8	+0.8	.....	+0.4	.....	+0.8	
8	16 yr., 6 mo.	.....	.....	.....	+1.1	.....	+0.5	+0.4	+0.2	+0.9	.....	+0.5	+1.1	
9	18 yr., 5 mo.	.....	.....	.....	.....	+1.1	+1.3	+1.6	+1.5	+1.3	+1.3	+0.7	+1.6	
10	17 yr., 6 mo.	.....	.....	.....	.....	−3.0	.....	−1.2	.....	.....	−0.2	+0.2	−3.0	Menstruation began late
11	16 yr., 7 mo.	.....	.....	.....	.....	+1.7	.....	0	.....	0	+1.8	.....	+1.8	
12	17 yr., 7 mo.	.....	.....	.....	.....	.....	.....	+0.5	+1.3	+0.4	0	−0.5	+1.3	
13	16 yr., 9 mo.	.....	.....	.....	.....	.....	+1.2	.....	+2.1	+1.7	+1.4	+1.2	+2.1	
14	18 yr., 8 mo.	.....	.....	.....	.....	.....	.....	.....	−1.0	−0.4	−0.4	+0.5	−1.1	
15	19 yr., 4 mo.	.....	.....	.....	.....	.....	.....	.....	−0.2	.....	+0.2	0	±0.2	
16	19 yr.	.....	.....	.....	.....	.....	.....	.....	.....	+1.1	+0.5	+0.4	+1.1	

Average maximum error	1.4 in. (3.56 cm.)
50 per cent under	1.2 in. (3.05 cm.)
75 per cent under	1.8 in. (4.57 cm.)
90 per cent under	2.5 in. (6.35 cm.)
Range	3.0 in. (7.62 cm.)

Totals for Tables 1 and 2 (33 Girls)

Average maximum error	1.92 in. (4.88 cm.)
50 per cent under	1.6 in. (4.06 cm.)
75 per cent under	1.8 in. (4.57 cm.)
90 per cent under	3.0 in. (7.62 cm.)
Range	5.2 in. (13.21 cm.)

90 per cent under	2.5 in. (6.35 cm.)
Range	3.0 in. (7.62 cm.)

90 per cent under	3.0 in. (7.62 cm.)
Range	5.2 in. (13.21 cm.)

TABLE 3.—*Errors in Height Prediction of Boys*

Patient	Final Age	5 Yr.	6 Yr.	7 Yr.	8 Yr.	9 Yr.	10 Yr.	11 Yr.	12 Yr.	13 Yr.	14 Yr.	15 Yr.	16 Yr.	Maximum Error	Comment
1	19 yr., 1 mo.	+0.5	−0.9	−0.8	+0.5	−1.4	+0.9	.....	.....	.....	.....	+2.0	.....	+2.0	
2	22 yr.	.....	−0.5	0	0	+0.5	+0.6	.....	+0.6	+0.1	.....	+1.0	.....	+1.0	(?) Hypopituitary; bone age, 17 yr. at 15 yr., 4 mo.
3	18 yr., 7 mo.	.....	−1.0	−1.0	.....	.....	.....	.....	+1.5	.....	+3.6	+2.5	+1.0	+3.6	Italian
4	18 yr., 3 mo.	.....	−0.5	+0.3	+0.5	+0.6	.....	.....	.....	.....	+2.5	+1.8	+1.5	+2.5	Italian
5	20 yr., 10 mo.	.....	.....	.....	.....	.....	+2.8	+2.8	+3.0	+2.8	+2.8	.....	.....	+3.0	(?) Hypopituitary; bone age, 11 yr. at 10.5 yr.
6	17 yr., 7 mo.	.....	.....	.....	.....	−1.0	.....	.....	−0.8	+0.2	+0.5	+1.2	+1.2	+1.2	
7	17 yr., 6 mo.	.....	.....	+0.6	0	0	+1.0	.....	−0.3	.....	+0.6	+0.4	.....	+1.0	
8	17 yr., 9 mo.	.....	.....	.....	.....	0	0	+1.4	+1.4	+0.6	0	0	+0.6	+1.4	
9	17 yr., 10 mo.	.....	.....	.....	.....	.....	.....	.....	0	−1.2	−1.2	−1.2	.....	−1.2	
10	17 yr., 7 mo.	.....	.....	.....	.....	−1.0	−0.2	+0.5	−0.5	−1.0	−1.4	−0.8	−1.8	−1.4	
11	17 yr., 8 mo.	.....	.....	−2.4	.....	.....	.....	.....	.....	+1.4	.....	+2.0	+0.8	−2.4	
12	18 yr., 10 mo.	.....	.....	.....	.....	.....	.....	.....	.....	.....	−1.8	−1.8	.....	−1.8	Bone age, 14 yr., 3 mo. at 15.8 yr.; corrected to −0.8

Average maximum error	1.87 in. (4.75 cm.)
50 per cent	1.4 in. (3.56 cm.)
75 per cent	2.5 in. (6.35 cm.)
90 per cent	3.6 in. (9.14 cm.)
Largest error	3.6 in. (9.14 cm.)

In light of these observations, we reexamined our data and found that the greatest errors in the prediction of height were made in the cases of girls who began menstruation at ages other than 13½ years. It was noted that in the cases of those who began menstruation earlier than 13½ years, the predictions were always greater than the height actually attained. The reverse was true for those who began menstruation after the age of 13½ years. In 17 of the 33 girls, the age at which menstruation began was known. In these cases, the difference between the age of 13½ years and the age at which menstruation began was added to the chronologic age if menstruation was early and subtracted if it was late. Other errors were determined in a similar manner by adjusting and plotting the various ages on the graphs (table 1). This changed the percentile standings so that the errors in height prediction were markedly decreased, especially within two to three years of the time of menstruation. In this series, it was noted also that each child tended to maintain either a positive or a negative error throughout the period of growth. This indicates that a child usually remains advanced or retarded in sexual maturation during the entire period of growth. In our group of children, a few bone age studies had been made during the growth period; this decreased the errors in the prediction of final height. In the boys, bone maturation ages were available in 3 cases, and these gave a similar correction of the error in prediction of height at the time the bone age had been taken.

A fairly accurate prognostication of final height can be made in the individual child by using the percentile chart. It can be made more accurate by determination of the degree of skeletal maturation and by substituting the bone maturation age for the chronologic age. According to Todd's standards, the bone age can be determined with a deviation of not more than six months. Therefore, if the bone age is more than six months advanced or retarded from the chronologic age, the bone age should be substituted for the chronologic age.

An accurate estimate of the probable final stature of any child is of value to the orthopedic surgeon in planning operative treatment in cases of inequality of leg length. For instance, shortening of the leg or epiphysial arrest might be unwise in a child who promises to be extremely short at the completion of growth. On the other hand, in a child who is likely to be extremely tall, shortening procedures would be preferable to lengthening ones because of the comparative simplicity of the shortening procedure.

PREDICTION OF THE ADULT PROPORTIONS OF THE FEMUR AND THE TIBIA TO STATURE IN THE INDIVIDUAL PATIENT

From available data, we can arrive at significant and useful conclusions regarding the prediction of the final proportions of the femur

TABLE 4.—*Errors in Height Prediction of Girls (Not Followed to Complete Growth) with Theoretic Correction of Chronologic Age of Menstruation of Thirteen and a Half Years*

Patient	Final Age	5 Yr.	6 Yr.*	7 Yr.	8 Yr.	9 Yr.	10 Yr.	11 Yr.	12 Yr.	13 Yr.	14 Yr.	15 Yr.	Maximum Error	Age at Which Menstruation Began	Comment
1	15 yr., 3 mo.	.....	.....	−0.9 −0.6	−0.9 −0.5	+0.9 −0.5	+1.0 −0.3	+2.0 +0.6	+2.5 +0.8	+1.5 +0.5	+1.5 +0.6	+1.2 +0.7	+2.5 +0.8	12 yr., 4 mo.	
2	16 yr.	.....	.....	.....	+1.5 +0.6	.....	+2.0 +1.5	.....	+2.9 +1.8	+2.2 +1.5	+1.5 +0.8	+0.7 +0.4	+2.9 +1.8	13 yr.	
3	15 yr., 10 mo.	.....	.....	.....	.....	+3.0 +1.8	+3.0 +1.6	+3.0 +1.6	+3.0 +1.8	+3.0 +2.0	+1.8 +1.0	+1.5 +1.0	+3.0 +2.0	12 yr., 5 mo.	
4	15 yr., 9 mo.	.....	.....	.....	.....	.....	.....	+2.2 +1.6	+2.4 +1.6	+2.6 +1.8	+1.8 +1.5	+0.9 +0.5	+2.6 +1.8	13 yr., 1 mo.	Spanish
5	16 yr.	.....	.....	.....	.....	.....	.....	.....	+1.8 +0.8	+0.8 +0.4	+1.2 +0.8	+0.9 +0.6	+1.8 +0.8	13 yr.	
6	14 yr., 4 mo.	.....	.....	.....	.....	.....	.....	+2.6 −1.0	+2.7 −0.4	+2.3 +0.8	+1.8 +0.4	.....	+2.7 −1.0	11.6 yr.	
7	15 yr., 5 mo.	.....	+1.5 −1.5	+2.1 −0.7	+2.3 −0.5	+2.7 −0.3	.....	+4.2 +0.5	+3.1 +0.5	+2.4 +0.4	+2.0 +0.4	+1.0 +0.1	+4.2 −1.5	11.9 yr.	
8	15 yr., 3 mo.	.....	−0.4	.....	+1.1	+0.7	.....	+0.5	−0.3	−0.3	+0.3	+1.0	+1.1	?	
9	14 yr., 10 mo.	.....	.....	.....	.....	+2.0	+2.5	+2.5	+2.5	+2.4	+2.0	.....	+2.5	?	Rheumatoid arthritis
10	14 yr., 8 mo.	.....	.....	.....	.....	+2.5	+2.8	+2.8	.....	.....	.....	+1.5	+2.8	?	
11	15 yr., 11 mo.	.....	.....	.....	.....	.....	+3.0	+3.0	+3.2	+2.8	+1.4	+1.0	+3.2	?	Chinese; tuberculosis
12	15 yr., 3 mo.	.....	.....	.....	.....	.....	.....	−1.1	−0.7	+0.7	+1.2	+0.8	+1.2	13 yr., 5 mo.	Rheumatic fever

Errors in Height Prediction in the 8 Cases in Which the Age of the Beginning of Menstruation is Known

Average maximum error	2.61 in. (6.63 cm.)
50 per cent under	2.6 in. (6.60 cm.)
90 per cent under	3.0 in. (7.62 cm.)
Largest error	4.2 in. (10.67 cm.)

Errors in Height Prediction Corrected by Considering the Age at Which Menstruation Began as 13.5 Years

Average maximum error	1.36 in. (3.45 cm.)
50 per cent under	1.2 in. (3.05 cm.)
90 per cent under	1.8 in. (4.57 cm.)
Largest error	2.0 in. (5.08 cm.)

* Lower figures represent corrections.

and the tibia to the total stature of individual patients even though a complete teleroentgenographic study of the growth of these two bones has never been made in individual children.

Meredith [9] and Boynton [24] showed that the average variation of the proportions of total leg length to stature is small from the ages of 7 to 17 years (fig. 6). Schwerz [14] likewise found that the average variation of the proportions of the femur and the tibia to stature was small from the ages of 6 to 14 years, the limits of his material (fig. 4).

Schultz [13] noted, in comparing Negro and white fetuses, that the proportion of the length of the legs to the body was larger in the Negro. The same is true of Negro adults as compared with white adults. If racial trends in bodily proportions are laid down in infancy, this should be true also of individual bodily proportions. Maresh and Deming [25] took teleroentgenographic measurements of infants from birth to the

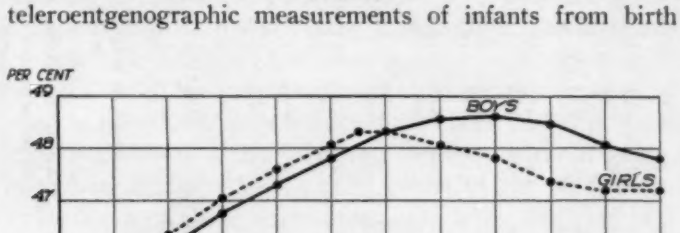

Fig. 6.—Leg length as percentage of stature as drawn from data of Meredith.

age of 6 months. They found that the curves of growth for the bones of different children were parallel during the entire period and that in each child the relation in length between any two bones of the body remained constant in a remarkable number of cases.

Baldwin studied the relation between the sitting height and the standing height of individual patients between the ages of 10 and 15 years. He found that this relation was remarkably constant and that the children maintained their group rating in this proportion more closely than in any other bodily characteristic. If this is true for the relation

24. Boynton, B.: The Physical Growth of Girls: A Study of the Rhythm of Physical Growth from Anthropometric Measurements on Girls Between Birth and Eighteen Years, Studies in Child Welfare, Iowa City, University of Iowa, 1936, vol. 12, no. 4.

25. Maresh, N. M., and Deming, J.: The Growth of the Long Bones in Eighty Infants: Roentgenograms Versus Anthropometry, Child Development **10**:91 (June) 1939.

between the sitting height and the standing height, it must be true for the length of the legs, since this measurement was derived by subtraction of the sitting height from the total stature. Wallis confirmed this in a study of 54 boys and 49 girls who were followed individually for five years between the ages of 3 and 12 years.[12] She concluded that the person's constitutional type tends to persist in spite of variation in age through at least seven years of preadolescent growth, the limits of her material. In addition, she noted that the children maintained their own bodily pattern more closely than that of their parents.

In view of these data, it may be concluded that a child maintains the relative proportions of the femur and the tibia to stature with only small age variations. For this reason, the surgeon can estimate the probable adult proportions of these bones to stature by taking a child's present proportions and adding small age changes.

The subtable in figure 5 is a table of additions to the present percentage of the femur and the tibia to the stature. These figures are to be added to the calculated present percentages of these bones to stature according to the age and the sex in order to determine the probable adult percentage of the length of the femur and the tibia to the stature in a child. This table was compiled from the incomplete data of Meredith, Boynton, Schwerz and Davenport and will be modified as more accurate information on the growth of children is accumulated. For our purpose, these changes by age are so small that the final length of the femur and the tibia could be determined fairly accurately in the later postnatal period of growth by multiplying the present proportions of these bones to the stature by the predicted height. However, because these age changes, though small, are definite, they should be considered in order to increase the accuracy of our calculations. By the use of this table, the final proportions of the femur and the tibia to the stature will probably be predicted with an error of less than 0.5 per cent in the prediction of the final length of either the femur or tibia.

PERCENTAGE OF GROWTH FROM THE PROXIMAL AND THE DISTAL EPIPHYSIAL CARTILAGES

At the present time, the only work available to determine the actual percentage of growth from the ends of the long bones is that of Digby, Bisgard and Bisgard [26] and Payton.[27] Digby's method (fig. 7 *A*) was used in an unstated number of dried human bones. The Bisgards implanted metal shots in living goats, and the figures obtained were

26. Bisgard, J. D., and Bisgard, M. E.: Longitudinal Growth of Long Bones, Arch. Surg. **31**:569 (Oct.) 1935.

27. Payton, C. G.: The Growth in Length of the Long Bones in the Madder-Fed Pig, J. Anat. **66**:414 (April) 1932.

checked against Digby's method in dried bones (fig. 7 *B*). Payton fed madder to growing pigs. The relative similarity of the figures obtained by these methods in human beings, goats and pigs is interesting

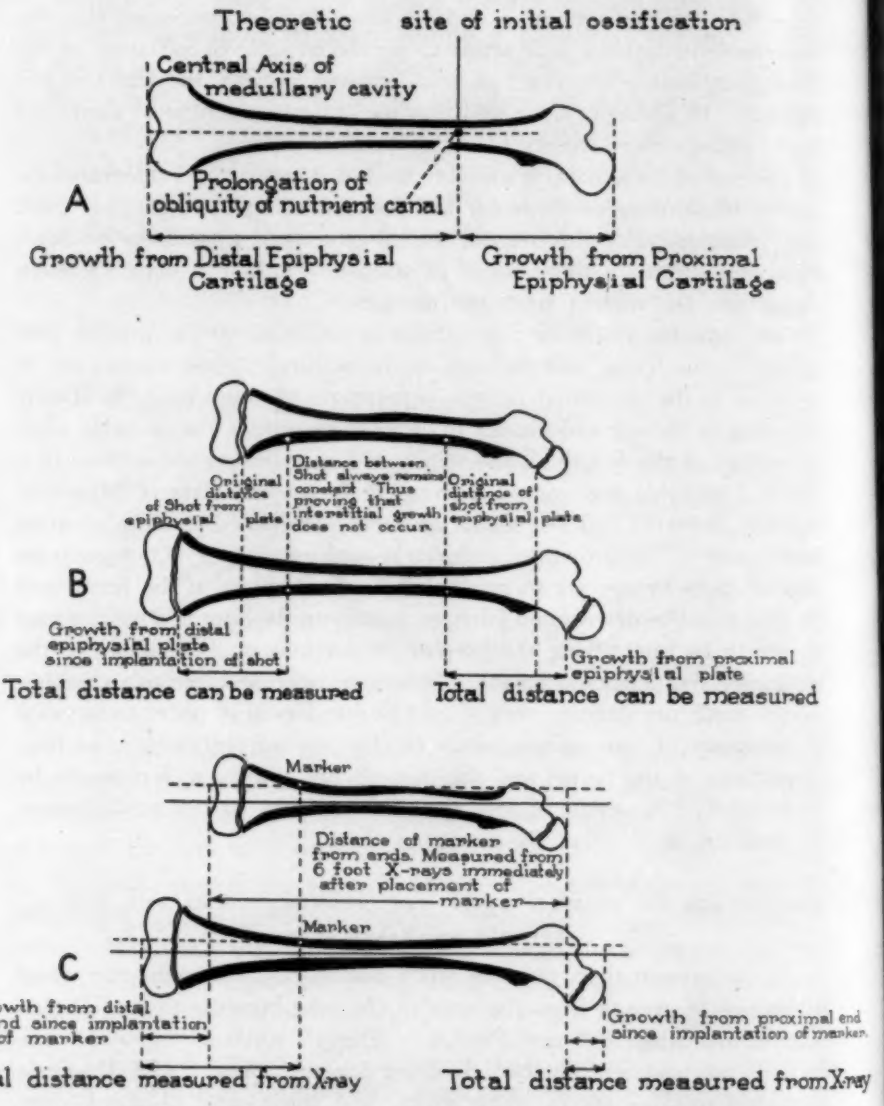
Theoretic site of initial ossification
Central Axis of medullary cavity
A
Prolongation of obliquity of nutrient canal
Growth from Distal Epiphysial Cartilage
Growth from Proximal Epiphysial Cartilage
B
Original distance of Shot from epiphysial plate
Distance between Shot always remains constant Thus proving that interstitial growth does not occur
Original distance of shot from epiphysial plate
Growth from distal epiphysial plate since implantation of shot
Growth from proximal epiphysial plate
Total distance can be measured
Total distance can be measured
Marker
Distance of marker from ends. Measured from 6 foot X-rays immediately after placement of marker
Marker
C
Growth from distal end since implantation of marker
Growth from proximal end since implantation of marker
Total distance measured from X-ray
Total distance measured from X-ray

Fig. 7.—Diagram illustrating various methods of determining the percentage of growth from each end of the long bones. *A*, Digby's nutrient canal method of calculating percentage of growth from each end of a long bone. *B*, Bisgards' shot method of determining percentage of growth from each epiphysial cartilage. *C*, method of determining the percentage of growth from each end of the bones in growing children.

(table 5). Although Digby's method is open to considerable criticism,[28] it is probably fairly accurate for human beings.

In goats and pigs, it is noted that in prenatal and early postnatal life the percentages contributed from each end of a bone are more nearly equal than in later life. However, from the work of the Bisgards it appears that the relative percentages of growth from each end of the bone are constant during the postnatal period. In human beings, there is some indication that the proportion of growth from each end of the bone is somewhat more equal in prenatal life and early postnatal life than in later postnatal life. In 1 instance, bismuth had been prescribed for a pregnant woman during the last five months of pregnancy. This resulted in transverse lines being laid down across the long bones of the infant. These lines showed that the proportion of growth for the

TABLE 5.—*Comparison of Percentage Growth from Various Epiphyses as Determined by Various Authors*

			Femur		Tibia		Humerus		Radius		Ulna	
Author	Subject	Method	Proximal	Distal	Proximal	Distal	Proximal	Distal	Proximal	Distal	Proximal	Distal
Digby [7].....	Human	Nutrient canal	31.2	68.9	57.1	42.9	80.8	19.2	25	75	18.6	81.4
Bisgard and Bisgard [26]	Goats	Shots to epiphysial plate	35.8	64.2	54.5	45.2	82	18	25.5	74.5	18.8	81.2
	Goats	Nutrient canal	32.7	67.3	56	44	81.7	18.3	25.5	74.5	19.6	80.4
Payton [28]...	Pigs	Madder fed	37.2	62.8	71.8	28.2	78.8	21.2	20.8	79.2	31	69

last five months of prenatal life in the upper and lower ends of the femur was 46:54 and 50:50 for the upper and lower ends of the tibia. In the first five months of postnatal life, the proportion of growth was 40.6:59.3 for the femur and 38:62 for the tibia. From lines of arrested growth, Harris determined that the proportion of growth in the tibia of a child between the ages of 3½ and 5½ years was 51.4:48.6. The greatest amount occurred at the upper end.[29] By the use of vitallium markers, which will be described in a later paragraph, in the case of a Negro boy, we determined that the percentage for the femur was 37:63 and for the tibia 53:47 between the ages of 5 and 5½ years (fig. 7*C* and 14). From lines of arrested growth in a Chinese girl, we found that the percentage for the tibia was 55:45 between the ages of 4 and

28. Payton, C. G.: The Position of the Nutrient Foramen and Direction of the Nutrient Canal in the Long Bones of the Madder Fed Pig, J. Anat. **68**:500 (July) 1934.

29. Harris, H. A.: The Growth of the Long Bones in Childhood, Arch. Int. Med. **38**:785 (Dec.) 1926.

6½ years. In another patient, two lines of arrested growth resulting from two successive injuries at known times were found in the metaphysis of the normal femur. In this case we were able to determine that the percentage of growth from the distal end of the femur was 70 per cent between the ages of 8 and 10 years (fig. 8). This figure is close to Digby's figures. At the present time our experience convinces us that the following percentages of growth may be accepted until more exact studies have been made on human beings by the implantation of metal markers in the long bones (fig. 7 *C* and 14):

Femur: proximal end, 30 per cent; distal end, 70 per cent
Tibia: proximal end, 55 per cent; distal end, 45 per cent

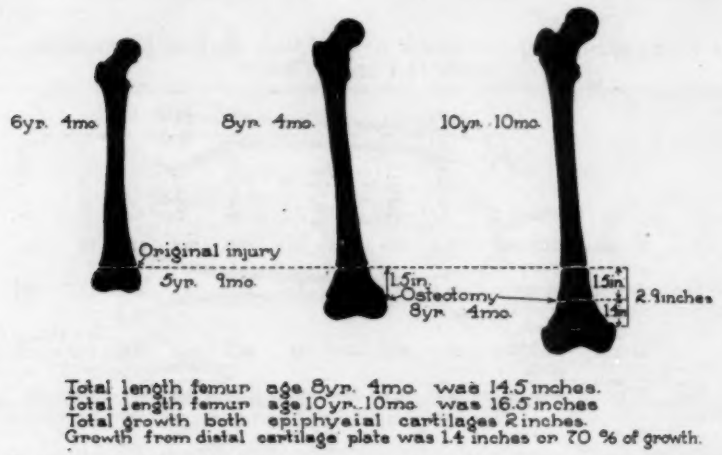

Fig. 8.—Estimation of the percentage of growth from the epiphysial cartilages of a normal femur; calculation is made from lines of arrested growth appearing after two specific injuries.

As mentioned before, we believe that growth should be estimated separately from the respective ends of each bone because of the changes in the relative rates of growth of the femur and the tibia. Since this method of estimating the normal growth of the bones has been developed only recently, we have not had an opportunity for follow-up work in a sufficient number of cases to check its accuracy in the individual child.

The following case reports and accompanying diagrams illustrate cases in which the growth or the loss of growth from individual epiphyses of the long bones has been measured. In these cases, we were able to compare the actual loss of length with the amount estimated to occur from these centers by reversing our method. In other words, we have calculated the expected length of the bones at an earlier age from the patient's measurements at the present time.

REPORT OF CASES

CASE 1.—R. J. (fig. 9), a boy 10 years and 10 months of age, suffered a severe injury at the age of 5 years and 9 months; at that time a line of arrested growth was laid down in the femur. At 8 years and 4 months, a major operation caused another line of arrested growth to appear in the same bone. Measurements based on the lines of arrested growth showed that the growth from the distal femur had been: 1.5 inches (3.81 cm.) from the age of 5 years and 9 months to the age of 8 years and 4 months and 1.4 inches (3.57 cm.) from the age of 8 years and 4 months to the age of 10 years and 10 months.

Fig. 9.—Diagram made from roentgenograms showing the amount of longitudinal growth contributed by the distal femoral epiphysis as shown by lines of arrested growth appearing after specific injuries.

Other available measurements were:

Age	Height	Length of Femur	Femoral Percentage of Stature
5 yr., 9 mo.	46.5 in. (118.11 cm.)	Not known	....
8 yr., 4 mo.	52.75 in. (133.99 cm.)	14.5 in. (36.83 cm.)	27.5
10 yr., 10 mo.	59.5 in. (151.13 cm.)	16.5 in. (41.91 cm.)	27.9

If we had seen the patient at the age of 8 years and 4 months, the growth at the age of 10 years and 10 months could have been calculated in the following manner:

The femoral percentage at 8 years and 4 months was 27.5. The height at 10 years and 10 months was estimated to be 58.6 inches (148.82 cm.), and the femoral percentage was expected to increase to 28 per cent. Therefore, the calculated femoral length at 10 years and 10 months would have been 28 per cent × 58.6 or

16.4 inches (41.67 cm.). This compared closely with the actual length that the femur attained. The growth from the distal part of the femur would have been 1.9 × 0.7 or 1.3 inches (3.3 cm.). This is close to the actual growth of 1.4 inches (3.55 cm.) from the distal part of the femur.

It is possible to calculate backward from the age of 10 years and 10 months to the age of 5 years and 9 months in order to compare the expected growth with the amount which actually occurred. This is shown in figure 9. The calculated growth was 2.5 inches (6.35 cm.) as compared with the actual growth of 2.9 inches (7.37 cm.), an error of 0.4 inches (1.02 cm.) for a period of five years of growth.

Case 2.—C. V. (fig. 10), a man 24 years of age, at the age of 6 years had suffered a fracture involving the lateral portion of the distal epiphysis of the femur. Owing to the premature fusion of the lateral portion of this epiphysis, severe valgus deformity of the knee developed. Teleroentgenograms were taken of both femurs. Comparative measurements revealed a loss of 5.2 inches (13.21 cm.) in growth from the distal femoral epiphysis between the age of 6 years and full

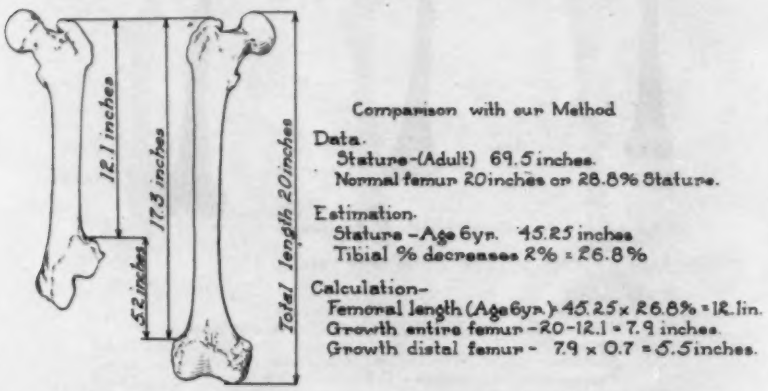
12.1 inches
17.3 inches
5.2 inches
Total length 20 inches
Comparison with our Method
Data.
Stature-(Adult) 69.5 inches.
Normal femur 20 inches or 28.8% Stature.
Estimation.
Stature - Age 6 yr. 45.25 inches
Tibial % decreases 2% = 26.8%
Calculation-
Femoral length (Age 6 yr.) 45.25 x 26.8% = 12.1 in.
Growth entire femur - 20 - 12.1 = 7.9 inches.
Growth distal femur - 7.9 x 0.7 = 5.5 inches.

Fig. 10.—Diagrams from teleroentgenograms demonstrating deformity and loss of length after premature closure of the lateral portion of the distal femoral epiphysis from age of 6 to full growth.

growth. Available measurements of this patient's height in early life were as follows:

3 yr., 6 mo.—42 in. (106.68 cm.), estimated from final height and percentile chart for stature to have been 39.5 in. (100.33 cm.);

4 yr., 6 mo.—43 in. (109.22 cm.), estimated from final height and percentile chart for stature to have been 42 in. (106.68 cm.);

10 yr., 6 mo.—55.5 in. (140.97 cm.), estimated from final height and percentile chart for stature to have been 54.6 in. (138.68 cm.).

From the patient's height and the length of the normal femur at the present time, the theoretic growth from the distal epiphysis of the femur (fig. 10) would have been 5.5 inches (13.97 cm.), an error of 0.3 inches (.762 cm.) over a period of eleven or twelve years of growth.

Case 3.—L. H. (fig. 11), a young man 17 years and 8 months of age, at the age of 12 years had sustained a fracture involving the lateral portion of the distal epiphysis of the right femur. Valgus deformity occurred as a result of premature fusion of the lateral portion of the epiphysial plate.

In September 1936, a cuneiform osteotomy of the femur was performed; the base of this included the medial side of the distal epiphysial cartilage. This resulted in fusion of the entire epiphysial cartilage plate. This osteotomy gave fair correction of the deformity but did not change the length of the femur on the lateral side.

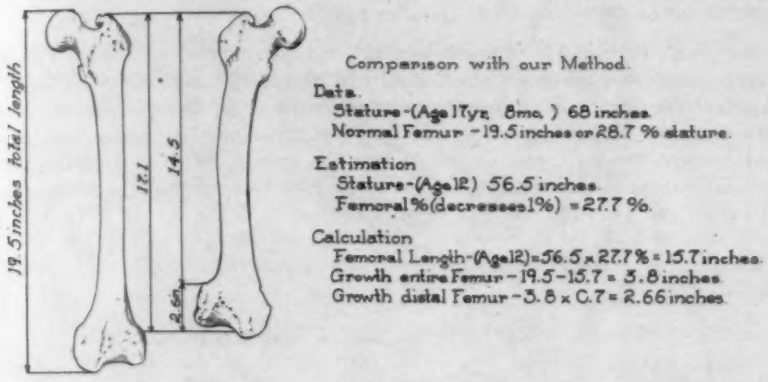
19.5 inches total length
13.1
14.5
2.6cm.
Comparison with our Method
Data.
Stature-(Age 17yr. 8mo.) 68 inches.
Normal Femur - 19.5 inches or 28.7 % stature.
Estimation
Stature-(Age 12) 56.5 inches.
Femoral % (decreases 1%) = 27.7 %.
Calculation
Femoral Length-(Age 12) = 56.5 x 27.7 % = 15.7 inches.
Growth entire Femur - 19.5 - 15.7 = 3.8 inches.
Growth distal Femur - 3.8 x 0.7 = 2.66 inches.

Fig. 11.—Diagrams from teleroentgenograms demonstrating deformity and loss of length after premature closure of the lateral portion of the distal femoral epiphysis from the age of 12 to the age of 17 years and 8 months. When the patient was 14 years of age, closing osteotomy was performed on the medial side; this effected a decrease in the deformity but did not bring about a decrease in length on the lateral side.

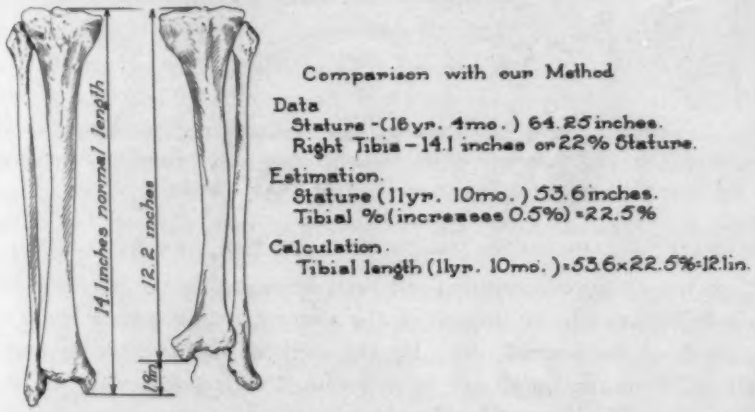
14 inches normal length
12.2 inches
1.8cm.
Comparison with our Method
Data
Stature - (16 yr. 4 mo.) 64.25 inches.
Right Tibia - 14.1 inches or 22 % Stature.
Estimation.
Stature (11 yr. 10 mo.) 53.6 inches.
Tibial % (increases 0.5%) = 22.5 %
Calculation.
Tibial length (11 yr. 10 mo.) = 53.6 x 22.5 % = 12.1 in.

Fig. 12.—Diagrams from teleroentgenograms demonstrating actual loss of length after closure of both epiphyses of the tibia from the age of 11 years and 10 months to the age of 16 years and 4 months.

Comparative measurements taken from the greater trochanter to the lateral epicondyle of each femur showed a loss of 2.6 inches (6.6 cm.) in length. From the length of the normal femur and the patient's height at the present time, the estimated growth from the distal epiphysial cartilage of the femur was 2.66 inches (6.76 cm.).

Case 4.—E. M., (fig. 12), a youth 16 years and 4 months of age, at the age of 11 years and 10 months suffered severe burns of his left leg which became infected. Osteomyelitis occurred and destroyed the distal epiphysis of the tibia. At the time of writing, the length of the medial side of the left tibia is 12.2 inches (31 cm.), which probably approximates the length at the time of the burn. By our method, the length of the tibia at the age of 11 years and 10 months was calculated to be 12.1 inches (30.73 cm.).

Case 5.—C. P. (fig. 13), a youth 16 years and 9 months of age, at the age of 10 years sustained a fracture which destroyed the medial portion of the distal epiphysis of the tibia. Measurements revealed a loss of 1.5 inches (3.81 cm.) of growth from the medial side of the tibia. From the length of the normal tibia and his present height, it was calculated that the growth which took place from the normal epiphysial cartilage plate of the lower tibia between the ages of 10 years and 16 years and 9 months was 1.35 inches (3.43 cm.).

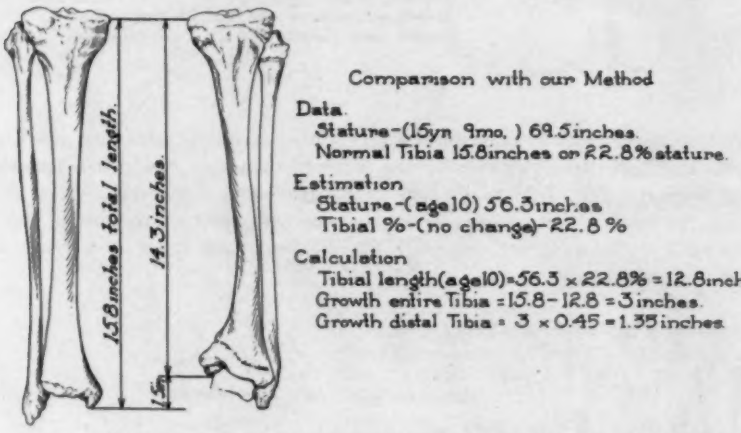

Fig. 13.—Diagrams from teleroentgenograms demonstrating deformity and loss of length after premature closure of the medial portion of the distal tibial epiphysis from the age of 10 years to the age of 15 years and 9 months.

ESTIMATE OF THE EXPECTED GROWTH OF THE ABNORMAL LIMB

It should be emphasized that any final inequality in the length of the legs is dependent on the growth of the abnormal limb with relation to the growth of the normal one. By the method outlined, the expected growth of the normal limb can be determined with a reasonable degree of accuracy. This is a valuable aid in estimating the growth of the shorter leg. In every case, a careful study should be made of the mechanism which produces the inequality and its relation to the growth of the individual epiphyses. There are three such mechanisms: (1) disturbances confined to specific epiphysial plates; (2) disturbances affecting the rate of growth of all of the epiphyses of the limb; (3) mechanical loss in length.

Disturbances Confined to Specific Epiphysial Plates.—(*a*) Complete Premature Closure of One or More Epiphyses: Complete premature closure of one or more epiphyses is usually a result of trauma, such as a fracture crossing the epiphysial cartilage or a crushing injury of this structure. It may also be caused by roentgen therapy or operative procedures in the vicinity or at the site of the epiphysis. Destruction of the epiphysial cartilage by tuberculosis or osteomyelitis is frequent, but involvement of the epiphyses by tumors is less common.

Complete premature closure of an epiphysis during the period of growth results in the loss of the longitudinal growth which that epiphysis would have contributed. Calculation as to the loss of growth is a simple matter because the undamaged centers are usually growing at a normal rate. Therefore, the final length will be the normal growth minus the expected growth from the closed epiphysis which may be calculated entirely on the normal expectancy of growth in that bone.

Operative closure of the corresponding epiphysial plate on the sound bone will immediately fix the inequality and prevent it from increasing. This inequality may be decreased by the fusion of other epiphysial plates of the normal leg. The calculations are made on the basis of the growth of the normal leg except possibly in those cases caused by infection. In children 6 to 8 years of age, an injury involving the lower epiphysis of the femur may cause a loss in growth of 4 to 6 inches (10.16 to 15.24 cm.). At such an early age, it is probably unwise to fuse the corresponding epiphysis of the normal limb, especially if the child is likely to become a short adult. In these cases, leg lengthening may be indicated.

(*b*) Incomplete Closure of One Epiphysial Cartilage Plate: Incomplete or partial closure of an epiphysis is generally due to injury. Angular deformities develop with the growth of the undisturbed portion of the epiphysis. Epiphysial arrest of the entire plate will prevent an increase in deformity. In certain instances, however, in which the loss resulting from this procedure would be too great, a series of osteotomies may be planned in order to gain length from this unilateral growth.

(*c*) Alteration in the Rate of Growth of One Epiphysis: Increase in the rate of growth of a single epiphysis may be caused by damage from operative intervention or a decrease in its blood supply from the same cause. Alteration in the rate of growth may occur also when there is juxtaepiphysial osteomyelitis. An increase in the rate of growth of an epiphysial plate may be due to increased vascularity from localized osteomyelitis or a tumor of the hemangiomatous type in the metaphysial region. If the lower epiphysis of the femur had been so affected in early childhood, severe inequality might result. To determine the relative rates of growth of the two sides, metal markers may be placed in the shafts of both femurs and tibias for the purpose of recording measure-

ments. If the inequality in length already present is equal to the expected growth of the corresponding epiphysial plate, then this epiphysis may be fused and the inequality kept from increasing.

Disturbances Affecting the Rate of Growth of All the Epiphysial Plates of the Limb.—(*a*) Epiphysial Plates Intact with Growth at a Decreased Rate in Comparison with the Normal Limb: This is the most common mechanism producing inequality in the length of legs. A number of factors may play a part, the most important of which is defective circulation with lowered local temperature and disuse. This mechanism frequently follows poliomyelitis but may be caused also by any long-standing disabling condition in the extremity. Great difficulty is often encountered in these cases in estimating the comparative rates of growth of the normal and abnormal limbs. In a general way, it is known that the loss of growth of the limb is related to a decrease of local temperature which, in turn, is probbaly caused by vasomotor changes. Furthermore, the shortening is usually greater in cases with the greatest degree of muscular paralysis. The tibia ordinarily shows the largest loss of growth since the most marked vasomotor changes and residual paralysis are generally found in the distal portion of the extremity. Despite these general impressions, it is not yet determined whether the rate of growth is affected as a whole or whether there is a disturbance in the normal ratios of growth between the proximal and distal ends of the long bones. As a rule, such calculations can be made only in rare instances in which lines of arrested growth appear in the long bones. Unfortunately, accurate calculations cannot often be made from these lines because they are seldom of sufficient density and the time of their appearance is frequently indefinite. For this reason, we have devised a simple method by which small markers are inserted subcutaneously into the cortex of the shafts of the femurs and the tibias. These markers can be put through the soft parts and implanted in the bones without incision. The marker is the end of a vitallium stylet which is introduced through a hypodermic needle. The stylet has a notch about $\frac{5}{16}$ inch (0.8 cm.) from its point. It is placed within the needle with its notch projecting just beyond the end of the needle. The needle and the stylet are fixed in a drill chuck, turned through the soft parts and drilled into the bone. The depth is limited by the cuff formed by the end of the hypodermic needle. The chuck is then removed, and with the needle in place, the stylet is bent until it breaks at its notch, leaving only the point in the bone. The markers remain permanently for the measurement of comparative rates of growth of the individual epiphyses. After the introduction of the markers, teleroentgenograms are taken. Subsequent teleroentgenograms at regular intervals are compared with the original films and give the exact amounts of growth from each end

of the bones, thus permitting definite calculations of comparative rates of growth from the epiphyses (figs. 7 *C* and 14). In this way, epiphysial arrest may be carried out in a more accurate manner. Increasing study by this means will add much information to the store of knowledge regarding both normal and abnormal growth.

Some children are seen so near the completion of the period of growth that no time is allowed for such studies. If the expected growth

Fig. 14.—Teleroentgenograms of a Negro boy who had poliomyelitis at the age of 1 year with residual paralysis of the right leg. Vitallium markers were implanted in both femurs and tibias for the determination of the relative rates of growth of the individual epiphyses of the two legs. *A*, at 5 years of age, immediately after the implantation of the markers. *B*, at 5½ years of age.

from one or more epiphyses of the normal limb is less than or equal to the discrepancy in length already present, the epiphyses contributing this amount may be fused. The result of this procedure will depend on the rate of growth of the epiphyses of the short leg.

In many cases in which this mechanism has been present since an early age, i. e., in children from 10 to 12 years of age who had polio-

myelitis from infancy and in whom there is only 2 to 3 inches (5 to 7.6 cm.) of shortening, a period of observation is unnecessary. Simple analysis of the difference in the length of the bones in comparison with the probable growth since the onset of the disease, shows that the actual growth rate of the abnormal limb is so close to that of the normal limb that for all practical purposes the expected growth of the shorter leg may be calculated on the basis of the growth of the normal leg. From such considerations, a proper time for epiphysial arrest may be determined. If it is obvious that equalization cannot be obtained by epiphysial arrest alone, other procedures such as leg lengthening or leg shortening may be planned.

In children of short stature with healed joint disease, especially disease of the hip which has resulted in fusion of the joint, the shorter limb may be lengthened. Both the operation itself and the postoperative lengthening in such cases are relatively simple, and the functional results are good because the extremity is stable and the muscular power is usually normal.

(*b*) Epiphysial Plates Intact with Growth at an Increased Rate as Compared to the Normal Limb: This mechnaism of altered growth may be caused by congenital hemangioma or post-traumatic arteriovenous aneurysm. It may also follow low grade infections of a chronic nature, such as osteomyelitis, syphilitic lesions of the bone or prolonged soft tissue infection. The factors which produce an augmented rate of growth are undoubtedly increased vascularity and increased local temperature of the limb.

Mechanical Inequality.—In the third group are placed those cases in which there is a loss in the length of the bone because of overriding or angulation in healed fractures, destruction of bony substance by infection or tumor or by a dislocation of the hip. To equalize the length of the legs in these cases, either reduction of the dislocation of the hip or correction of the angular deformity by osteotomy is generally indicated. If a considerable shortening still remains, other measures may be planned for the equalization of leg length. If all the epiphysial cartilages of the shorter leg are growing at a normal rate, closure of the epiphyses of the sound limb should give final equality in the length of the legs. In most of these cases, however, there is often a decrease in the rate of growth of the epiphysial cartilage or a loss of growth from its destruction. This may be determined from roentgenograms and by careful measurement from teleroentgenograms. If the determination of the rates of growth cannot be made from the teleroentgenograms alone, markers may be used. If, however, the discrepancy is great and the patient is of such age that further growth is limited, epiphysial arrest may be safely performed on the basis of the normal rates of growth.

SUMMARY

A practical method is here presented for estimating the final height and the proportionate lengths of the femur and the tibia in individual children. This method can be effectively employed in planning operative procedures which aim to equalize the length of the extremities. By use of the skeletal maturation age, errors are eliminated which might occur if the chronologic age alone is employed.

When comparative rates of growth of the extremities are indeterminable by this method, we have found the metal markers previously described and placed in the bone by a special technic to be of great value.

Parnassus and Third Avenues.

EARLY CARCINOMA IN THE HYPERPLASTIC THYROID

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Carcinoma of the thyroid has been the subject of numerous excellent contributions in which its various aspects and phases have been fully discussed. Information regarding the pathologic nature, the diagnosis and the treatment of this type of tumor has been greatly increased. Nevertheless, there remain many problems to be solved and large and small gaps in the knowledge of it to be filled.

A case recently observed at this hospital has drawn our attention to the well known, but curious and unexplained, fact that carcinoma of the thyroid is exceedingly rare with diffuse hyperplasia of this gland.

Coller [1] found a gland hyperplastic only once among 90 cases of thyroid carcinoma. Pemberton [2] observed diffuse hyperplasia in 10 instances of 774 cases of thyroid cancer, and Friedell,[3] in 12 among 412 cases. Four cases of carcinoma in a hyperplastic gland were mentioned by Clute and Warren.[4] No such simultaneous occurrence has been recorded in the large series of Wilson,[5] Herbst,[6] Simpson,[7] Brenizer and McKnight [8] and Crile.[9]

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1. Coller, F. A.: Adenoma and Cancer of the Thyroid: A Study of Their Relation in Ninety Epithelial Neoplasms of the Thyroid, J. A. M. A. **92**:457-462 (Feb. 9) 1929.

2. Pemberton, J. de J.: Malignant Disease of the Thyroid Gland: A Clinical Consideration, Ann. Surg. **87**:369-377 (March) 1928.

3. Friedell, M. T.: Hyperthyroidism and Adenocarcinoma of the Thyroid, Arch. Surg. **43**:386-396 (Sept.) 1941.

4. Clute, M., and Warren, S.: The Prognosis of Thyroid Cancer, Surg., Gynec. & Obst. **60**:861-874 (April) 1935.

5. Wilson, L. B.: Malignant Tumors of the Thyroid, Ann. Surg. **74**:129-184 (Aug.) 1921.

6. Herbst, W. P.: Malignant Tumors of the Thyroid, Ann. Surg. **79**:488-494 (April) 1924.

(Footnotes continued on next page)

It is obvious from these figures that the epithelium of the hyperplastic thyroid has extremely little, if any, tendency toward malignant degeneration. The reason for such behavior is not understood, and no attempt at explanation has been made. On the other hand, it is beginning to be understood why carcinoma does, although infrequently, arise in a hyperplastic gland. Clute and Warren [4] stated their belief that in such cases, carcinoma originates in a small adenoma within the hyperplastic gland. Similar evidence has been furnished by Goetsch.[10] By careful study of multiple blocks of tissue, he was able to demonstrate that miliary adenoma is considerably more frequent in the hyperplastic gland than was heretofore thought and to trace the origin of at least part of the carcinomas to these small adenomas. His observations were confirmed by Graham.[11] According to Graham, these small subcapsular scirrhus-like lesions of papillary or adenomatous structure infiltrate the adjacent tissue but apparently do not invade blood vessels. They do not seem to originate in adenoma. In concluding, Graham suggested that what has been considered a harmless lesion may have a malignant phase.

The case hereinafter reported forms, in our opinion, a connecting link between the early lesions described by Goetsch and Graham and the diffuse carcinoma in the hyperplastic thyroid, in which the histogenesis of the tumor is completely obscured.

REPORT OF A CASE

Mrs. O. W. R., a 55 year old white woman, was admitted to the surgical service on two occasions. The first time she was seen in June 1941, when a diagnosis of thyrotoxic heart disease with congestive failure was made. Even after adequate preparation, she was considered too poor a risk for operation, and she was allowed to go home. She returned after one month because of increasing nervousness, tremor of the hands, swelling of the ankles and a suffocating feeling in the right side of the chest.

She was somewhat emaciated. The skin was moist, and her eyes protruded slightly. She had a fine tremor of both hands. The heart was enlarged to the left. The blood pressure was 180 systolic and 118 diastolic; the pulse rate was

7. Simpson, W. M.: A Clinical and Pathological Study of Fifty-Five Malignant Neoplasms of the Thyroid, Ann. Clin. Med. **4**:643-667 (Feb.) 1926.

8. Brenizer, A. G., and McKnight, R. B.: True Adenoma of the Thyroid Gland and Their Relation to Cancer, Tr. Am. A. Study Goiter, 1940, pp. 176-190.

9. Crile, G., Jr.: Hyperthyroidism Associated with Malignant Tumors of the Thyroid Gland, Surg., Gynec. & Obst. **62**:995-999 (June) 1936.

10. Goetsch, E.: Incipient Carcinoma Occurring in Exophthalmic Goiter and Originating in Adenoma, Tr. Am. A. Study Goiter, 1940, pp. 191-205.

11. Graham, A., in discussion on Goetsch.[10]

124 per minute. The liver and the spleen were enlarged, and the ankles were swollen. Electrocardiographic examination showed sinus tachycardia and a low T wave. The basal metabolic rate was + 53 per cent. The laboratory findings were essentially negative. The blood cholesterol content was 150 mg. per hundred cubic centimeters.

The diagnosis was hyperthyroidism complicating essential hypertension, enlargement of the heart and hyposystolic heart failure.

She was given a diet in which salt and fluid were restricted, and compound solution of iodine U. S. P. (Lugol's solution), digitalis and mercupurin were administered.

Fig. 1.—Photomicrograph showing an area of characteristic hyperplasia.

A week after admission she had an episode which was considered due to a pulmonary infarct. She recovered from this rather quickly, but her improvement on conservative therapy was not satisfactory. It was then felt that the symptoms of hyperthyroidism were definitely not secondary to the essential hypertension but that this was a combination of both thyroid and vascular disease and that the patient should have the benefit of thyroidectomy. Total thyroidectomy was performed on August 18. The operation did not present any particular difficulties.

The postoperative course was uneventful. The patient has since been seen on various occasions. At the time of writing, moderate hypothyroidism has developed. The cardiac decompensation was not noticeably improved by thyroidectomy, and at

the last examination, in December, it had taken a turn for the worse. There was no evidence of local recurrence of the thyroid carcinoma, nor was there regional or distant metastasis.

Microscopic Examination.—Both thyroid lobes were slightly enlarged. The capsule was somewhat thickened. The tissue was firm, with a dull dark brownish red beefy cut surface, which showed rather distinct small lobulation. In one lobe, a roughly spherical whitish gray firm scirrhus-like area with a softer yellowish center was located immediately beneath the capsule nearer to one pole. It measured 1.5 cm. in diameter.

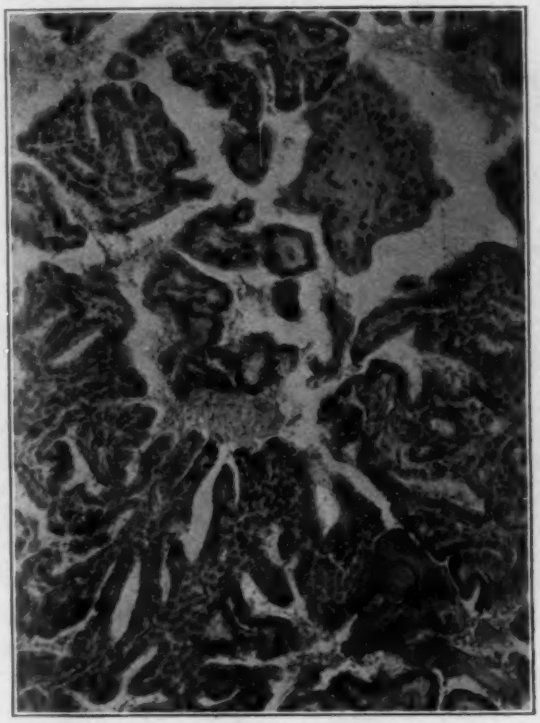

Fig. 2.—Photomicrograph of papillary adenocarcinoma of the thyroid. This specimen is from the tumor inside the fibrous capsule.

Microscopic Examination.—The thyroid was hyperplastic, but to a varying degree. While large areas presented the characteristic picture of hyperplasia (fig. 1), in others the follicles were more regular, the epithelium lower, the colloid more abundant and acidophilic and less vacuolated. Lymphocytic infiltration was practically absent. The stroma was slightly increased.

Numerous blocks were taken from the area described before and cut at levels. The lesion appeared to be papillary adenocarcinoma of high differentiation (fig. 2).

The epithelium of the papillae formed one layer, and the cellular and nuclear structure was fairly regular. The tumor was completely surrounded by a thick fibrous capsule which contained small vessels and lymphatic tissue forming follicle-like aggregations. Round cells were also scattered loosely through the capsule. No mature or immature thyroid tissue was found inside the capsule. The papillary tumor invaded the capsule at numerous places and extended into the adjacent thyroid tissue, appearing there as a diffuse adenocarcinoma with narrow irregular, sometimes solid, glands. The cellular and nuclear structure, however, was, here too, fairly regular. In several places the lymphatic tissue and the small blood vessels of the capsule were invaded by the tumor (fig. 3).

Diagnosis.—The diagnosis was papillary adenocarcinoma in hyperplastic thyroid.

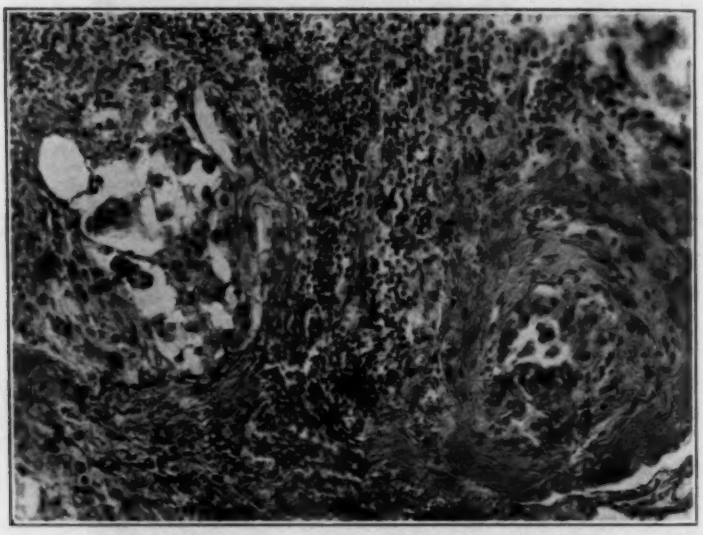

Fig. 3.—Photomicrograph of a tumor invading the lymphatic tissue and a vessel of the fibrous capsule.

COMMENT

We believe that the carcinoma originated in what probably was one of the small adenomas in the hyperplastic thyroid which were described by Goetsch.[10] In the present case, the carcinoma was already at a more advanced stage and had destroyed the original adenoma, but the complete encapsulation, the marked contrast to the thyroid gland proper and the absence of other areas of nodular involution surely support our opinion strongly.

Papillary overgrowth of epithelium, it is true, may occasionally be observed in hyperplastic goiters of long standing, but then such lesions are not so clearly separated from the thyroid tissue and surely are not malignant.

While one may hesitate to consider any papillary thyroid tumor malignant—in view of the regularity of the cellular pattern and the apparently good prognosis of many such lesions—we believe that the histologic criteria of malignancy of a thyroid tumor were fulfilled in the present case. Unquestionably, the papillary pattern represents the first step toward dedifferentiation of the thyroid epithelium. Together with the vessel-invading adenomas, the papillary tumors are classified by most observers in one group in contrast to the adenocarcinomas and undifferentiated tumors. Such a distinction is justified on clinical grounds, but there are no distinct histologic boundaries since the difference in pattern and extension are only expression of a varying degree of differentiation of what is basically always an adenocarcinoma arising from thyroid epithelium.[12] In our case, the tumor was papillary inside of the capsule but was a frank adenocarcinoma where it invaded the capsule and the thyroid proper. It is easy to imagine that with further spread of the tumor, sooner or later, depending on its rate of growth, all landmarks would become obliterated and that it would become entirely impossible to recognize whether the then diffuse adenocarcinoma originated in a small adenoma or in the gland tissue proper.

The importance of adenoma for the genesis of carcinoma is well established for the nodular goiter. It is beyond the scope of this paper to enter the much discussed argument: true adenoma versus nodular involution. The incidence of carcinoma in nodular (adenomatous) goiter is so much higher than in the smooth enlargements of the gland that a causal relation is certain.

The relative infrequency of adenoma in diffuse hyperplasia of the thyroid may account for the rarity of carcinoma in such glands, but it is probable that the adenoma represents the source of the carcinoma in all phases of goiter whether the morphologic equivalent of dysfunction is the hyperplastic or the nodular goiter.

In our case the hyperthyroidism was unquestionably due to the hyperplastic thyroid tissue and not to the tumor. That thyroid carcinoma itself may produce symptoms of hyperthyroidism was denied by Marine,[13] Eisen,[14] Pemberton,[2] Crile[9] and others, while Simpson[7] described cases of thyroid carcinoma producing hyperthyroidism and Friedell[8] reported that in 57 of 412 cases of thyroid carcinoma, a

12. Broders, A. C.: Surgical Pathology of the Thyroid Gland, Tr. Am. A. Study Goiter, 1940, pp. 288-300.

13. Marine, D.: Experimental Observations on the Effects of Administration of Iodine in Three Cases of Thyroid Carcinoma (Two Human, One Canine), Arch. Int. Med. **11**:288-299 (March) 1913.

14. Eisen, D.: Malignant Tumors of the Thyroid: An Analysis of Seven Cases with a Study of the Structure and Function of the Metastases, Am. J. M. Sc. **170**: 61-74 (July) 1925.

clinical diagnosis of hyperthyroidism was made, but only in a few cases could the thyroid itself be eliminated as the probable source of the thyrotoxic symptoms. That tumors of other endocrine glands may show secretory activity is well known. For the thyroid, the problem apparently remains unsettled for the time being.

Graham pointed out that small incipient carcinoma of the thyroid does not cause clinical symptoms and cannot be diagnosed before operation. According to him, removal by operation is sufficient, and irradiation is not indicated. We have not given radiation treatment to our patient, and she seems to be cured of the carcinoma. However, a single observation and the short time elapsed after operation do not permit of an opinion.

SUMMARY

A case of carcinoma of the thyroid arising in an adenoma in a hyperplastic gland is presented. The infrequent simultaneous occurrence of thyroid carcinoma and diffuse hyperplasia of the gland is discussed. The importance of miliary adenoma in the hyperplastic gland for the formation of carcinoma is stressed.

ABSORPTION OF SURGICAL GUT (CATGUT)

IV. RECOMMENDATIONS FOR ABSORBABILITY AND DIGESTIBILITY SPECIFICATIONS

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The Committee of Revision of the United States Pharmacopeia recently caused to be adopted a new terminology for the designation and the labeling of catgut. It is of interest that the term surgical gut will hereafter be officially used in place of the misnomer "catgut" to designate sheep intestine which has been prepared for surgical use. ("Catgut," however, is to be included in the Pharmacopeia as a synonym, with special character indicated by its being quoted and used with qualifying words, as in the term "surgical 'catgut'" or "'catgut' suture.") Four types of surgical gut are officially recognized. These are called types A, B, C and D. Type A is plain untreated surgical gut, and types B, C and D represent varying grades of treated surgical gut, i. e., those given mild, medium and prolonged treatment, respectively. These treated grades of surgical gut are generally labeled type B: mild chromic surgical gut; type C: medium chromic surgical gut; and type D: extra chromic surgical gut.

It is implied that the several types of treated surgical gut shall have imparted to them by chromicizing, tanning or other means a graduated and relatively greater degree of resistance to absorption than is generally possessed by plain untreated surgical gut. No specific statements have as yet been made as to what degree of resistance to digestion or absorption these three types of treated surgical gut might be expected to possess.

It is possible that the various manufacturers of surgical gut have at least for the present carried over their chromicizing specifications of what was formerly labeled ten day, twenty day and forty day chromic catgut for what is now labeled type B: mild chromic surgical gut, type C: medium chromic surgical gut and type D: extra chromic surgical gut, respectively. They could hardly be expected to do otherwise in the absence of uniform absorbability and digestibility specifications for the several types of treated surgical gut.

It should not be overlooked that a progressive catgut manufacturer has taken the lead for some time in attempting to eliminate from the

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labels on catgut any precise statement regarding the absorption time in the tissues, except in a rather general way, such as ten to twenty or thirty to forty days, which was added to the label parenthetically. It is a fitting tribute to this manufacurer that the Committee of Revision of the United States Pharmacopeia should pattern the recently adopted terminology for catgut (viz., medium chromic and extra chromic surgical gut) after that which has been advocated by this company for a long time.

TABLE 1.—*Recommendations for the Absorbability and Digestibility Specifications of Surgical Gut (Catgut)*

	Type A: Plain Surgical Gut (Untreated)	Type B: Mild Chromic Surgical Gut (Mild Treatment)	Type C: Medium Chromic Surgical Gut (Medium Treatment)	Type D: Extra Chromic Surgical Gut (Prolonged Treatment)
Absorbability				
Duration of tensile strength in the tissues				
Average	(AAA)* 5 days	(AAB) 8 days	(AAC) 12 days	(AAD) 18 days
Theoretic minimum range	(TRAA) 3 to 6½ days	(TRAB) 6½ to 10 days	(TRAC) 10 to 15 days	(TRAD) 15 to 25 days
Probable maximum range	(PRAA) 2 to 10 days	(PRAB) 5 to 12 days	(PRAC) 8 to 20 days	(PRAD) 12 to 30 days
Ultimate complete absorption in the tissues	Rapid (1 to 3 weeks)	Rapid or Intermediate	Intermediate or Slow	Slow (3 to 6 mo.)
Digestibility				
Average	(ADA)	(ADB) 1.6 ADA	(ADC) 2.5 ADA	(ADD) 3.5 ADA
Theoretic minimum range	(TRDA) 0.6 to 1.3 ADA	(TRDB) 1.3 to 2 ADA	(TRDC) 2 to 3 ADA	(TRDD) 3 to 5 ADA
Probable maximum range	(PRDA) 0.3 to 2 ADA	(PRDB) 1 to 2.5 ADA	(PRDC) 1.5 to 4 ADA	(PRDD) 2.5 to 6 ADA

* For the sake of convenience, the various specifications for the four types of surgical gut can be abbreviated in the following manner: AAA, average absorbability of type A; TRAB, theoretic range of absorbability of type B; PRAC, probable range of absorbability of type C, and so on. ADA represents the average digestion time of type A: plain untreated surgical gut in vitro determined by enzyme digestion test and expressed in terms of hours.

In the light of clinical and experimental observations made over a period of five years in this study of the absorption of surgical gut, recommendations are hereby submitted for the absorbability and digestibility specifications of the four types of surgical gut now officially recognized (table 1). These recommendations are based on over 4,000 observations on the absorbability of surgical gut in the tissues [1] and

1. Jenkins, H. P.: A Clinical Study of Catgut in Relation to Abdominal Wound Disruption, Surg., Gynec. & Obst. **64**:648, 1937. Jenkins, H. P., and Hrdina, L. S.: Absorption of Surgical Gut (Catgut): I. The Decline in Tensile Strength in the Tissues, Arch. Surg. **44**:881 (May) 1942. Jenkins, H. P.; Hrdina, L. S.; Owens, F. W., and Swisher, F. M.: Absorption of Surgical Gut (Catgut): III. Duration in the Tissues After Loss of Tensile Strength, ibid. **45**:74 (July) 1942.

about 3,200 observations on the digestibility of surgical gut in vitro, using pepsin [2] or trypsin [3] as a digestive agent.

In the elaboration of specifications for surgical gut, a number of points must be taken into consideration; these arise from the standpoint of the product, the manufacturer, the surgeon and the patient's tissues. In the first place, it must be recognized that the absorptive qualities of surgical gut cannot be precisely specified. The inherent resistance of the raw product, obtained from various sources, which is used by the manufacturer, may vary from time to time. The precision methods of chromicizing or tanning may thus be negated to some extent. Another factor is the variability in the absorption of the surgical gut in the tissues of different patients or experimental animals.

Because of such variability aspects, the specifications for surgical gut should be made with a reasonable amount of leeway rather than with too much precision. The average duration of tensile strength listed in the specifications (AA, average absorbability) should be considered only as a rather gross average. The theoretic minimum range of absorbability (TRA) should be considered that range of duration of tensile strength which it is most desirable to maintain for the several types of surgical gut. The probable maximum range of absorbability (PRA) is that range of duration of tensile strength which might be reasonably expected if the manufacturers made an effort to standardize their products to the average absorbability (AA) or the theoretic range of absorbability (TRA) which has been outlined for the several types.

The specifications which are presented for the absorbability of the various types of surgical gut are somewhat in conflict with previous conventional concepts of catgut absorption. The concept that twenty day chromic catgut was supposed to maintain its tensile strength for twenty days in the tissues and undergo complete absorption in three additional days has been somewhat altered by this study of the absorption of surgical gut. The mechanism of complete absorption has been found to present rather fundamental differences, depending on whether the cutgut was capable of resisting loss of tensile strength for more or less than ten days. Catgut which usually underwent loss of tensile strength in less than ten days was found to undergo rapid absorption by a polymorphonuclear leukocytic absorptive mechanism in less than three weeks. On the other hand, catgut which maintained its tensile strength beyond ten days was generally found to undergo slow absorption by a macro-

2. Jenkins, H. P., and Hrdina, L. S.: Absorption of Surgical Gut (Catgut): II. Pepsin Digestion Tests for Evaluation of Duration of Tensile Strength in the Tissues, Arch. Surg. **44**:984 (June) 1942.

3. The results of 500 pepsin digestion tests and 500 trypsin digestion tests not hitherto reported are to be made the subject of an additional article.

phage or histiocyte mechanism in three to six months. Between these two extremes of complete absorption there appeared to be an intermediately absorbed classification which corresponded with a duration of tensile strength of about ten days. The cellular mechanism in this intermediate type appeared to represent a combination of leukocytic and macrophage absorption. In both the intermediately and slowly absorbed types of surgical gut, it was generally observed that some initial leukocytic response was present. It is probable that the loss of tensile strength of surgical gut is due to the polymorphonuclear leukocytic mechanism, although macrophages or histiocytes are usually required to complete the absorption of the intermediately or slowly absorbed varieties of surgical gut.

There is obviously going to be some overlapping when one attempts to define in arbitrary terms the absorbability boundaries of four officially recognized types of surgical gut, because one can distinguish only three general categories from the biologic standpoint of complete absorption. Furthermore, one of these categories is none too distinct.

Therefore, in the specifications submitted for consideration, type A is presumed to be rapidly absorbable surgical gut from the standpoint of ultimate complete absorption, while type D is presumed to be of the slowly absorbed variety, which may require three to six months for completion of absorption. Type B may represent either rapidly or intermediately absorbed surgical gut, and type C may indicate either intermediate or slow absorption.

The specifications presented for type A, plain untreated surgical gut, from the standpoint of duration of tensile strength bring out the point that untreated surgical gut has a fairly wide range of absorbability. Although the average duration of tensile strength (AAA) is generally about five days in widely selected material, the range of absorbability credited to plain catgut (TRAA) may be stated at three to six and a half days, although not infrequently one encounters duration of tensile strength all the way from two to ten days (PRAA). As a matter of fact, some of the plain catgut which has been studied in this work on the absorption of surgical gut could fulfil the absorption specifications presented here for type B or even type C. There is nothing that has been found in this work which would lead one to condemn plain catgut which might be considered within the range of intermediately absorbed surgical gut. Indeed, there may be some virtue in intermediately absorbed plain catgut which has as yet not been clearly brought out. However, the manufacturer should be expected to indicate whether the plain catgut might be expected to be rapidly absorbed or intermediately absorbed.

The specifications presented for type C, medium chromic surgical gut, have been worked out from several standpoints. The establishment

of ten to fifteen days' duration of tensile strength as the theoretic range of absorbability (TRAC) is an attempt to reconcile what the average surgeon thought he was getting when he used the formerly labeled twenty day chromic catgut with what was more often the actual performance of the catgut in the tissues. It is probable that about ten days' duration of tensile strength (lower theoretic range of absorption of type C) is about as reasonable a specification to expect on the average for the larger sizes (no. 2 or no. 1) of this type of catgut. More extensively chromicized catgut in this size might lead to an undue number of complaints about draining sinuses, and less extensively chromicized surgical gut would not give a duration of tensile strength which was even theoretically safe for maintaining apposition of a normal healing wound.

Manufacturers have apparently found from experience that attention must be paid to the extent of chromicizing of the larger sizes. If a duration of tensile strength of as much as fifteen to twenty days is obtained with the no. 2 or no. 1 sizes, there may be a troublesome number of complaints about draining sinuses. These occur because the focal bulk of relatively highly resistant (to absorption) suture material has exceeded the tolerance of the tissues to foreign material at some point of concentration of the suture material. This is usually a large bulky knot which presumably fails to be encapsulated by the normal fibroblastic response of the tissues to foreign substances.

With a theoretic minimum standard of about ten days' duration of tensile strength for type C, manufacturers may still have some complaints about draining sinuses from the larger sizes of this type of surgical gut. However, this cannot be entirely avoided with large size suture material unless one resorts to such a minimal amount of chromicizing that the tensile strength becomes completely lost in five to eight days. If it is feasible to maintain a tensile strength duration of about ten days for these larger sizes, the completion of absorption might be expected to fall within the range of intermediately absorbed surgical gut. If a surgeon does not care whether the surgical gut which he uses for closure of fascial layers will maintain its tensile strength for a period of time which might be considered the minimum for reasonable safety in normal wound repair (ten days) and if he is much more concerned lest an occasional draining sinus occur, then he should be encouraged to use surgical gut which is not intended to be anything more than rapidly absorbed.

The smaller sizes of type C, medium chromic surgical gut, should probably be treated to an extent which will give them the upper theoretic range of absorbability of type C (TRAC). The tissues have a greater tolerance for the smaller sizes of relatively resistant (to absorption) suture material. Several manufacturers have found it feasible to chromicize their smaller sizes more extensively than their larger sizes. This

appears to have a reasonably sound biologic justification and should be encouraged among the various manufacturers. The extent to which one should chromicize the smaller sizes is of course open to divergence of opinion.

If the theoretic range of absorbability for type C (TRAC) is considered to be ten to fifteen days, it is reasonable to assume that in actual performance in the tissues, the probable range of absorbability (PRAC) will be about eight to twenty days.

For those who choose to use absorbable suture material which has been subjected to prolonged treatment to increase its resistance (to absorption) to approximately the maximum that can be reasonably tolerated by the tissues, type D, extra chromic surgical gut, should afford such an opportunity. This type should be expected to average about eighteen days' duration of tensile strength (AAD) and maintain a theoretic range of absorbability (TRAD) of fifteen to twenty-five days' duration of tensile strength. The probable range of absorbability (PRAD) which might be expected would hardly be less than twelve to thirty days. It is to be hoped of course that the manufacturers will tend to standardize the larger sizes at the lower theoretic range of absorbability of type D (TRAD) and the smaller sizes at the upper range in view of the graded tolerance of the tissues to the size of foreign material. Any surgical gut with the absorbability specifications just outlined would require three to six months for complete absorption.

Type D surgical gut is especially appropriate for use in patients who are expected to have some delay in wound healing from one cause or another. Also, it is desirable for operative procedures of considerable magnitude in which there is a greater incidence of complications of a nature which might put a strain on a healing abdominal wound.

This type of suture material (type D) affords a greater factor of safety for the healing sutured wound not only because of a longer duration of tensile strength but also because of the relatively minimal acute tissue reaction generally associated with the use of slowly absorbed surgical gut. It must not be overlooked, however, that the routine use of the larger sizes of this type of surgical gut may lead to a troublesome number of draining sinuses, just as is experienced with large sizes of silk. One must pay more attention to the fundamental surgical principle of minimizing focal bulk of foreign material in wounds when using highly resistant and slowly absorbed surgical gut than when using poorly resistant and rapidly absorbed suture material. If one chooses to resort to the smaller sizes (no. 0, no. 00 and no. 000) of this slowly absorbed type of material for fascial layers and to adopt interrupted technic instead of the conventional continuous suture (except in the peritoneum), one can obtain appreciable improvement in the reliability of wound closure. It is not necessary to resort to the exceedingly fine sizes of

suture material usually required for a successful silk technic (equivalent to no. 0000 or no. 00000) to avoid for the most part the foreign body reactions (draining sinuses) which one must occasionally expect from the use of highly resistant suture material.

Suture material which the various companies put up for gastrointestinal use should possess the maximum degree of resistance obtained from prolonged treatment. This is particularly essential because of the rapid digestive action of the gastrointestinal secretions on catgut. Some so-called gastrointestinal sutures have been found to be completely digested in less than twenty-four hours when incubated in the gastric contents recovered by siphonage from patients recently subjected to gastrointestinal anastomosis. It is doubtful whether surgeons will be easily persuaded to use absorbable suture material for gastrointestinal anastomoses unless a highly resistant suture is generally available from all companies for such use.

Type B, mild chromic surgical gut, is presumably for special situations which may require a mildly treated surgical gut that is theoretically intermediate in its absorbability between type A, untreated plain surgical gut, and type C, medium chromic surgical gut. It was found that plain catgut from some sources maintained its tensile strength for ten days in the tissues and that twenty day chromic catgut (now presumably type C) from certain sources was not infrequently found to undergo complete loss of tensile strength in less than ten days. In view of this observation one wonders whether type B is not an artificial and theoretic entity which in actual performance will merely be an overlap of type A and type C. It is possible that this type B classification has been carried over into the present United States Pharmacopeia out of deference to catgut tradition.

The specifications recommended for type B are an average duration of tensile strength (AAB) of about eight days, a theoretic range of absorbability (TRAB) of six and a half to ten days and a probable range of absorbability (PRAB) of five to twelve days' duration of tensile strength. The ultimate complete absorption of this type of surgical gut will presumably be rapid or intermediate, depending on whether the product was standardized at the lower or the upper bracket of the theoretic range of absorbability (TRAB).

The manufacturers should explore the possibilities of a mild treatment surgical gut in the smaller sizes which could be used for ligatures. Those who prefer the finer sizes for ligatures may occasionally experience the spontaneous untying of no. 000 or no. 0000 plain surgical gut on vessels from which bleeding might cause at least a serious hematoma if not a fatal issue. Relatively slight amounts of chromicizing appear to alter sufficiently the physical properties of surgical gut so that the untying phenomenon is relatively minimal. However, if the chromicizing

is too thorough and one obtains a slowly absorbed type of suture material, it will undoubtedly lead to difficulties if used routinely for ligatures in the superficial tissues.

The control of the absorbability of surgical gut has been carried out by manufacturers with the aid of digestion tests in vitro which are checked from time to time by animal implants. Nevertheless, considerable difference has been found in the absorbability of identically labeled products from the several companies. It is obvious that the manufacturers have not been entirely in accord regarding the absorbability or digestibility specifications which should reasonably be expected of the various types of surgical gut.

The most disputable aspect of specifications for surgical gut revolves about the relation which may exist between the digestibility in vitro and the absorbability in the tissues. The digestibility in vitro expressed in terms of digestion time in hours (or a convertible equivalent [4]) in an enzyme appears to represent the degree of resistance possessed by the surgical gut. It is entirely logical that arbitrary ranges of digestibility might be established which would indicate poor, slight, moderate and high degrees of resistance. These might be presumed to indicate what should be expected of types A, B, C and D, respectively, from the standpoint of resistance to absorption.

The main point about specifications for surgical gut is that the primary consideration should be the absorbability and the secondary consideration the digestibility. The latter should be considered only a means of accomplishing some degree of uniformity among the various manufacturers in their attempt to meet such absorbability specifications of the four types of surgical gut as appear to be in the best interest of the patient, the surgeon and the manufacturer.

The most reasonable kind of specification that could be adopted for the digestibility range of the various types of surgical gut would be the expression of such ranges in terms of the average digestibility of plain untreated gut (ADA). This suggestion is made because of the generally recognized variability in the digestive potency of enzymes. It is recognized also that there is a considerable variation in the digestibility of

4. Some manufacturers use a digestion test in which they incubate the catgut for a specified time and then test the residual tensile strength. These results can be converted into digestion time by the formula $\frac{T}{T\text{-}t} \times H = \text{Digestibility}$ (Hours of digestion time to end point), in which T is the original tensile strength; t is the residual tensile strength after a specified time in the digestive enzyme; H is the number of hours during which the surgical gut was exposed to the action of the digestive enzyme; T-t is the loss of tensile strength during digestion. This formula is subject to limitations and does not take into account the gradual loss of digestive potency of the enzyme. It affords a gross method of converting one type of result into digestion time.

untreated plain catgut from various sources. However, a wide selection from six or more companies, including sizes from no. 2 to no. 000, would undoubtedly give a general average which could be relied on to a greater extent than any fixed digestion time in an enzyme (unless the "intestinal fortitude" of subsequent generations of sheep should undergo appreciable fluctuation). Recent improvements in the standardization of digestive enzymes, however, may substantially decrease the variability formerly observed.

It is visualized that a central testing bureau should collect the various samples of plain untreated surgical gut (heat-sterilized finished product) and subject them to digestion in trypsin [5] or pepsin or both or any additional test which might be found useful. In addition, animal implants as well as clinical tests should be carried out under suitable arrangements with medical schools so that a satisfactory absorbability check can be made on the digestibility averages obtained. If one can secure clinical and experimental confirmation of a duration of tensile strength of approximately five days for a widely selected batch of plain catgut, one can be reasonably sure that the average digestibility of such plain catgut can be used as a basis for elaborating the digestibility specifications for the other types of surgical gut.

The information regarding the results of such tests and the samples of the surgical gut and the enzymes used should be made available to each company. Any one company may experience difficulty in obtaining standardization of their treated types (which should be expected to be comparable to that of other companies) on the basis of their untreated surgical gut if their particular source of raw material is subject to considerable variation in its inherent resistance. The only way one can obtain a satisfactory common base point from which to standardize surgical gut is to have some of the particular plain untreated surgical gut from which the average digestibility is ascertained as well as some of the same lot of the digestive enzymes used in these tests made available to each manufacturer.

In this way it would be possible for the various companies to have a common standard base point from which to work out the digestibility ranges by whatever particular routine of absorption control is used by the company. This could be accomplished by the application of correction or conversion factors to the company's particular kind of digestion tests. If a company has no way of knowing the exact digestive potency of the enzyme which is to be used by some central testing laboratory for checking the digestibility of its product, it is obvious that an unfair advantage may be taken of the company.

5. Kraissl, C. J., and Meleney, F. L.: A Method for Determining the Time of Catgut Digestion in Vitro, Surg., Gynec. & Obst. **59**:161, 1934. Kraissl, C. J.: Intrinsic Factors Altering the Absorption of Catgut, ibid. **63**:561, 1936.

Whatever type of digestion test is used by the central laboratory or the company should be such that the test is completed within the time that the enzyme retains most of its potency. The standardization of the minimum of the theoretic range of absorbability of type C, medium chromic surgical gut (TRAC), should be such, for example, that the digestion is completed within twenty-four hours. Digestion tests which are carried on for thirty-six hours or more with the same digestive solution will probably require some correction factor on account of the progressive attenuation of the digestive potency of the solution. Otherwise the digestion test may appear to indicate a greater degree of resistance than the suture actually possesses.

It is presumed that the primary function of the central testing laboratory should be to assist the manufacturers in maintaining a reasonably uniform range of absorbability of the several types of surgical gut rather than to coerce them into maintaining rigid arbitrary digestibility standards which may or may not represent the most desirable absorbability from the standpoint of the patient or the surgeon.

If the central testing laboratory cooperates with the various manufacturers in the standardizing of their products, it should be expected that the companies give to the central laboratory some details of the preparation and the manufacture of surgical gut which are not generally available to individual investigators. It is probable that digestion tests cannot be of as much service as desired unless information of a confidential nature is made available to some unprejudiced scientific group. Certain inconsistencies in the digestibility-absorbability relation of pepsin digestion tests in vitro to absorption tests in the tissues were encountered which could probably not be explained without recourse to such confidential information. This is undoubtedly true also for trypsin digestion tests.

If one obtains an average digestion time for a wide range of plain untreated surgical gut (ADA) and it has been demonstrated that samples of the same gut maintain an average duration of tensile strength of about five days (AAA), then one may proceed to formulate specifications for the digestibility of the various treated types of surgical gut.

Type A, plain untreated surgical gut, should be considered to have a theoretic range of digestibility of 0.6 to 1.3 times the average digestibility found for this type (TRDA — 0.6 to 1.3 ADA). The probable range of digestibility which might be expected would undoubtedly vary from 0.3 to 2 times the general average of digestibility of this type, as determined from widely selected material (PRDA — 0.3 to 2 ADA).

Type B, mild chromic surgical gut (mild treatment), should be considered to have a theoretic range of digestibility of 1.3 to 2 times the average digestibility of plain gut (TRDB — 1.3 to 2 ADA). The probable range of digestibility should be considered 1 to 2.5 times the average for plain surgical gut (PRDB — 1 to 2.5 ADA).

Type C, medium chromic surgical gut (medium treatment) should represent a theoretic range of digestibility of from 2 to 3 times the average digestibility of untreated gut (TRDC — 2 to 3 ADA). The probable range of digestibility which might be anticipated would be 1.5 to 4 times the average digestibility of plain surgical gut (PRDC — 1.5 to 4 ADA).

Type D, extra chromic surgical gut (prolonged treatment) should represent a theoretic range of 3 to 5 times the average digestibility of plain gut (TRDD — 3 to 5 ADA). The actual range of digestibility which might be expected would vary from 2.5 to 6 times the digestibility of untreated surgical gut (PRDD — 2.5 to 6 ADA).

The digestibility specifications submitted for the four types of surgical gut were elaborated in the light of correlation which was established in a large series of tests of the decline in tensile strength of surgical gut in the tissues and in acid pepsin. It was generally found in this work that plain catgut averaged about five days' duration of tensile strength. The catgut which had a duration of tensile strength of ten days in the tissues was found to have a digestion time in pepsin which was approximately twice that of the average for plain catgut. A fifteen day duration of tensile strength was equivalent to a digestion time which was three times that of plain catgut. A twenty day duration of tensile strength was generally associated with a digestion time in excess of four times that observed for plain catgut.

There were a number of inconsistencies in the digestibility-absorbability relation which were not easily explained. One brand of chromic catgut had a digestion-absorption ratio which was considerably out of line with that of any other chromic catgut. Digestibility standards on a product like this would be relatively valueless because a reasonably high digestion time might indicate a surgical gut which maintains its tensile strength in the tissues a much shorter time than would normally be expected of any other chromic catgut. Such factors as may contribute to the irritation of the tissues by the catgut or extraneous substances therein should, of course, be taken into consideration in attempts to evaluate discrepancies in the digestibility-absorbability relationship.

Certain brands of plain catgut were found to have a digestibility which was comparable to that of some brands of chromic catgut labeled twenty or forty day (now type C and type D) which maintained their tensile strength in the tissues for ten to fifteen days. This plain catgut, however, did not hold up as long in the tissues as the chromic catgut, although the digestibility was approximately the same. In addition, certain instances were observed in which plain catgut with a digestibility only slightly longer than the general average for plain catgut was found to have a duration of tensile strength in the tissues of about ten days. This was approximately twice the average absorbability of plain catgut.

On the basis of these specifications, the latter plain catgut would be classified as type A from the standpoint of digestibility, although its absorbability in the tissues would be considered either the upper range of type B or the lower range of type C. Its ultimate absorption would be considered in the intermediate category.

Instances such as these naturally make one hesitant to issue statements of too dogmatic a nature regarding the reliability of digestion tests in general or the ratio of digestibility to absorbability.

In view of the vagaries of surgical gut and the methods available for assaying its digestibility and absorbability, a reasonable degree of latitude should be permitted in whatever specifications are elaborated for the four types of surgical gut. Although one may be able to set up theoretic ranges of absorbability or digestibility which do not overlap on paper, it is obvious from the nature of surgical gut that in actual

TABLE 2.—*General Outline of Recommended Absorbability and Digestibility Specifications of Surgical Gut*

Type of Surgical Gut	Absorbability in the Tissues		Digestibility in Enzymes
	Duration of Tensile Strength	Complete Absorption	
Type A: plain surgical gut (untreated)	5 days	1 to 3 weeks	ADA
Type B: mild chromic surgical gut (mild treatment)	5 to 10 days	3 weeks to 3 mo.	1 to 2 × ADA
Type C: medium chromic surgical gut (medium treatment)	10 to 15 days	3 to 6 mo.	2 to 3 × ADA
Type D: extra chromic surgical gut (prolonged treatment)	15 to 25 days	6 mo.	3 to 5 × ADA

behavior in digestion tests or in the tissues there will be some degree of overlapping of the various theoretically bounded ranges of absorbability or digestibility. This should be taken into consideration and reasonable probable range of absorbability (PRA) and digestibility (PRD) incorporated in whatever specifications are ultimately elaborated.

SUMMARY AND CONCLUSIONS

The recommendations for the specifications on the absorbability and digestibility of surgical gut are briefly outlined in a general way in table 2.

The digestibility of types B, C and D are expressed in terms of the average digestibility of type A: plain untreated surgical gut (ADA). Thus, medium chromic surgical gut is presumed to have a digestion time which is twice to three times that observed for plain untreated surgical gut.

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